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THE DEFINITION OF INOPERABILITY OF CANCER*

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THE GREATEST MARGIN FOR ERROR in reporting the end-results of treatment for cancer may be found in the classification by the reporter of a regional or histologic type of cancer as operable or inoperable. The difficulty in correcting this fault is apparent when one realizes that three variable factors interplay in the pronouncement of a given cancer as non-resectable by any surgeon, namely: first, the condition of the patient as regards his age, the co-existence of degenerative diseases and the complications attendant on the presence of the cancer; second, the extent of the disease, meaning the degree of local or organic involvement, the specific organ or tissue implicated, the extension to and incorporation of neighboring viscera by the cancer and metastases to regional and distant sites; and third, the surgical philosophy, moral point of view, courage, and experience of the surgeon. In a large group of patients with generalized bone metastases, or diffuse involvement of lungs or liver, or peritoneal carcinosis or melanomatosis, the recognition and acceptance of inoperability is obvious to any physician. But there are too numerous other instances in which the definition of inoperability may be subjected to careful evaluation, criticism, and even condemnation.

THE POINT OF VIEW OF THE SURGEON

It is not the purpose of the writer to formulate a set of rules governing the behavior of the surgeon in a given circumstance, but rather to present certain arguments for extending the scope of operability for cancer. The very nature of this disease, the infirm and often aged patients in whom it so frequently develops, and the radical character of the numerous operations designed to combat it, all conspire to make the surgical treatment of cancer a hazardous venture for the patient and often an ordeal for the surgeon. With the knowledge of the inevitability of death from cancer that is not treated, it seems unnecessary to state that no surgeon would refuse a patient the slightest chance for cure or

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even relief because of a fear of criticism for failure or an unnatural pride in low figures for operative mortality. Nor should any surgeon attempt to play God and decide arbitrarily that a certain cancer patient had lived a sufficiently long life or that he had so few remaining years of even normal life expectancy that operation at best would hardly be worth while. We must take care in our weighty decisions concerning the denial or offering of a chance for life to a patient, that in our desire not to be the executioner, we achieve the same end-result by acting as an immoral judge. For example, if called upon to operate for a ruptured duodenal ulcer on a condemned criminal awaiting electrocution in the death row, the surgeon by his calling and in keeping with the Hippocratic Oath, operates with the same skill and renders just as meticulous postoperative care as if his patient were to live forever.

INOPERABILITY AND INCURABILITY

Many operations designed for the cure of cancer achieve in too many instances only a palliative end-result. If inoperability were an absolute state, and not a variable one, dependent in some cases on the criteria of the surgeon, the term would be synonymous with incurability. The unpredictable behavior of cancers and the immeasurable host resistance of organs and tissues to the growth of cancer combine in creating many intangible factors that make the early cancer occasionably incurable and the advanced cancer sometimes controllable. Assuming that a given cancer is not suitable for radiation therapy, operative removal becomes the only recourse. At the time of laparotomy, for example, a surgeon may be compelled to render judgment absolutely governing the life of the individual, the decision necessitating a matter of a few minutes as compared to days and weeks of courtroom deliberation by judge and jury. The closure of an abdominal wound on a cancer that is obviously hopeless is always done reluctantly, but the abandonment of an operation that is of questionable accomplishment must plague the conscientious surgeon for many sleepless hours and is one of the many reasons why he remains forever humble. He must worry whether his definition of inoperability is in his state of mind or moral courage or in the actual stage of the cancer. An aggressive attack on cancers presenting almost insuperable technical difficulties will sometimes result in palliative relief and occasionally in cures, but with mounting operative fatalities. Under these conditions, no one would impugn the good intent of the operator.

THE AGE OF THE CANCER PATIENT

One cannot become reconciled to the perverted point of view of some surgeons who are reluctant to operate on aged patients for major forms of cancer. Minor cancers that run a chronic course may not endanger the life of the patient, but a major cancer should be removed regardless of the age of the patient, providing it is technically possible and his physical state is not too precarious. The anatomic and physiologic age of the subject are infinitely more important than the chronologic age. At times, it would seem wiser to leave the actual age off the chart or for the patient conveniently to forget the

number of years he has lived if the knowledge of age alone unfavorably influences the surgeon; the fitness for the surgical ordeal would then be rightly determined by the true condition of the patient as judged by physical examination and laboratory tests. As examples, we have successfully performed hemi-colectomy for cancer of the cecum in two patients more than 80 years of age, in one of whom the operation was done under local anesthesia because of intussusception of long duration. A 92-year-old physician was cured of cancer about which he was genuinely concerned. The proverbial three score years and ten, however collectively applied, do not concern us when we reach that age, because most of us, including patients, live from day to day and year to year as if we were immortal. Some aged patients continue to possess a zest for life, and they merit every opportunity for cure or relief from otherwise fatal diseases that accidentally befall them; this is their privilege and their right regardless of advanced years just as their rights of franchise, speech and worship continue. Rather than refuse to operate, the surgeon may justifiably modify or simplify the character of the operation, for example, do a simple mastectomy under local anesthesia for cancers of the breast that have apparently not metastasized to the axilla.

THE CONDITION OF THE PATIENT

For every argument advanced against the decision to operate on any given patient, the irrefutable defense or rebuttal is the inevitable fatality from the untreated cancer. What would the surgeon do if confronted with an acute surgical emergency in the same patient, e. g., a ruptured duodenal ulcer or gangrenous extremity? A patient with cancer, who is gravely ill from the conjoined effects of the cancer and intercurrent diseases, of course would receive medical consultation, careful deliberation concerning the choice of anesthesia and meticulous preoperative preparation. The family should jointly assume with the surgeon the responsibility of undertaking to remove a major cancer in a patient who is a serious operative risk.

One illustrative case is that of an elderly woman, bedridden and almost helpless for years due to amyotrophic sclerosis, on whom a radical mastectomy was done. This chronic invalid was a most cheerful individual and the nucleus of a happy home with husband and children even more affectionate and concerned about her recovery and cure than is ordinarily the case. A 70 year old woman, seriously handicapped by heart disease, underwent an almost total gastrectomy for a huge leiomyosarcoma of the stomach. The jejunum was anastomosed to only a rim of stomach below the cardia. After a stormy convalescence, she recovered and now, 12 years later and 82 years old, is living and well except for the necessity of supportive treatment for her heart. An elderly woman entered the Memorial Hospital with a leiomyosarcoma of the uterus so large that it filled the entire abdomen and extended up as far as the epigastrium. She was in severe heart failure, did not respond to medical treatment, and was classified as inoperable by cardiologists who warned us not to attempt any surgical procedure. On the other hand, she

was experiencing hemorrhages of increasing severity. Because she could not lie recumbent, the operation was done in a modified Fowler's position; and under local anesthesia, an incision was made from the pubis almost to the ensiform cartilage. A pan-hysterectomy was done under local anesthesia including a liberal vaginal cuff. She was discharged from the hospital two weeks later with greatly improved cardiac compensation due, we thought, to the removal of this massive tumor.

THE STAGE AND EXTENT OF THE CANCER

The inoperability of an abdominal cancer is unquestioned in the presence of extensive hepatic metastases or peritoneal carcinosis. If a patient, on laparotomy, is found to have a few metastases in the liver without hepatic dysfunction or hard, irremovable retroperitoneal lymph nodes, one may still proceed with the removal of a cancer of the stomach, colon, or rectum, because experience has shown that gastric, colonic, or rectal resection is the best palliative measure for such cancers, though admittedly incurable. Here again, clinical judgment must influence one's decision, as nothing is gained by enabling a patient to live longer and suffer more. The measure of palliation accomplished by such resection is not necessarily the longer duration of life but the degree of freedom from distress. A lobectomy for a solitary metastasis in the lung in a patient who had experienced an amputation of an extremity for osteogenic sarcoma would have been considered meddlesome surgery a decade ago, but not in the light of the present day viewpoint. Three brief case reports will serve to illustrate an unpredictable salvage of life by surgical persistence in the face of overwhelming odds.

Case 1: D. D., a 24-year-old man, had a congenitally defective left hand, characterized by crossed fingers with contractures. For several years, a tumor had been slowly growing deep in the palmar space. An attempt at removal in another hospital was only partly successful; the specimen was reported by the pathologist as a neurosarcoma. An amputation through the forearm was done, followed in 17 months by recurrence in the stump; the arm was then amputated through the mid-humerus well above any clinical and microscopical evidence of the tumor. Within a year, another recurrence was observed and was treated by a disarticulation of the humerus. There was no evidence in the specimen of upward extension of the neurosarcoma. Subsequently, a mass was palpated in the axilla; aspiration biopsy was positive for sarcoma. The patient consented to an interscapulothoracic amputation which was performed on February 25, 1935. Surely, we reasoned, this will control or eradicate any possibility of recurrence of the sarcoma, but a few months later, another mass, somewhat fixed, was palpated in the lower neck. With determination but not with optimism, we performed a difficult dissection of this sarcoma from the brachial nerve plexus which it involved; the operation was terminated by inserting gold radon seeds in the wound. This last desperate surgical attempt (the sixth) was done 12 years ago. Since that time, the patient has gone to college, married, fathered two children, and become a successful teacher in a normal school. There has been no evidence of metastasis and no evidence of local recurrence of the neurosarcoma.

Case 2: N. H., a 30-year-old male, was referred to the Memorial Hospital in 1932 with a clinical diagnosis of melanoma of the skin of the chest. A bluish-black ulcerating tumor 2 cm. in diameter was seen in the pectoral region; there were large firm nodes in the corresponding axilla. The primary melanoma was surgically removed

and the axilla was dissected; the lymph nodes contained metastatic melanoma. Several months later, a rapidly-growing black, fungating tumor was observed on his bald scalp. It was removed and microscopically proved to be a malignant melanoma. In the course of the next year, numerous other bluish-black, rapidly-growing nodules 0.5 to 2 cm. in diameter appeared on his trunk, back, and arms. The clinical picture was typically that of disseminated melanoma in the skin, so much so that our professional colleagues in consultation commented on the futility of further surgical efforts. Nevertheless, we persisted in removing these tumors as they appeared, our only encouragement derived from the opinion of our pathologists, Dr. James Ewing and Dr. Fred Stewart, that these malignant melanomas had the peculiar features of new, independent, or primary growths rather than metastatic foci. The condition was further complicated at this time by the appearance of metastases in the opposite axillary lymph nodes, which were treated by radical axillary dissection. A total of 14 primary malignant melanomas were removed and both axillas were dissected for proved metastatic melanoma. It has been over ten years since the last operation, and the patient is well, without evidence of recurrence in this long interval. The satisfactory end-result is not due to any major surgical feat, but rather to the determined philosophy of treating cancer wherever it may be found.

Case 3: D. B., an 11-year-old southern schoolgirl, had a small nodule in the thyroid gland of which her parents had long been aware. Within two months after the somewhat precocious onset of menstruation, this nodule grew with alarming rapidity. A local surgeon was consulted and one of many palpable lymph nodes in the neck was removed for biopsy. It contained metastatic thyroid cancer. When we examined her, the thyroid cancer was infiltrative, fixed, and inoperable. Innumerable firm lymph nodes, involved by the disease, were felt throughout both cervical chains. Inasmuch as the cancer was inoperable, intensive treatment was given with the four gram radium element pack, supplemented by the interstitial deposition of gold radon seeds in measured tissue doses in the thyroid gland and remaining palpable lymph nodes. The dose was epidermicidal but effective in causing satisfactory regression of the cancer. Just before she was scheduled to return to her home in Alabama, she complained of headache, vomiting, and blurring of vision. Ophthalmoscopy revealed bilateral choked discs. A presumptive diagnosis of metastatic thyroid cancer to the brain was made. A ventriculogram showed the presence of a tumor encroaching on the lateral ventricle. At this time, the parents obtained conflicting advice, some physicians defining her condition as hopeless. Motivated by the same policy of continuing the treatment of cancer wherever found and influenced by the remote and even unlikely possibility of the intracranial tumor being unrelated, I urged craniotomy and surgical removal. This point of view was identical with that of the neurosurgeon, Dr. Byron Stookey, who performed the operation and removed the tumor which was situated in the choroid plexus of the lateral ventricle. To our dismay, but without surprise, the histologic study revealed metastatic thyroid cancer. This little girl matured gracefully, completed her academic and collegiate education, married, and became the mother of two children. She is now living and well 15 years after her treatment was completed.

INVOLVEMENT OF MULTIPLE ORGANS

One of the outstanding achievements in the surgical treatment of gastrointestinal cancer is the unexpected good result which frequently follows the removal of cancers that have become adherent to adjacent organs and are at first examination seemingly inoperable. The explanation lies in the fact that cancers of the stomach, colon, and rectum, which are papillary or polypoid in character, often become grossly infected and, as a consequence, the organ becomes adherent to adjacent viscera or structures. These tumors appear

technically irremovable and give the false impression of extension of the cancer beyond the confines of the organ primarily involved. By perseverance and meticulous dissection, associated at times with the sacrifice of a portion or the whole of the adjacent organ, the surgeon can often remove this growth successfully. The subsequent pathologic report, in many instances, will reveal that the cancer itself had not extended to involve the neighboring organ, and that the adhesions were of inflammatory character; in fact, the cancer itself may be classified as of relatively low-grade malignancy. I have known of numerous instances in which complications of this character were found, and yet no regional metastases to nodes were discovered on careful microscopical survey. These facts encourage one to attempt by every means possible the removal of cancers which are adherent to any structures that may be sacrificed by excision and continuity with the organ involved.

A. STOMACH

Although total gastrectomy had been attempted within a few years after Billroth's initial partial gastrectomy for cancer, the operation did not find popular acceptance by gastric surgeons until the past decade. It is now known that the entire stomach can be safely removed and the individual live thereafter without too great inconvenience and without too disturbing metabolic changes. On the Gastric Service of the Memorial Hospital, we have performed approximately 50 total gastrectomies for cancer and approximately 50 transthoracic resections of the lower esophagus and upper end of the stomach for cancers of the proximal gastric segment. In past years, the very location of the cancer, justaposed to the cardia, was sufficient to pronounce it inoperable in many hospitals, in consequence of which 8 to 10 per cent of all patients with gastric cancer were denied surgical intervention merely because of the accidental location of the cancer near the region of the cardiac orifice. The extension of the cancer to involve the esophagus, both below and above the diaphragm, called for a popularization of the operation of transthoracic, transdiaphragmatic esophago-gastrectomy. This procedure has now been well established. The end-results of this operation and the preoperative and postoperative management are so improved that these cancers can no longer be classified as inoperable because of location only. In these 100 cases of extremely radical surgery removal of gastric cancers, we have found many occasions to remove adjacent organs in whole or in part. Segments of the diaphragm, the entire spleen, variable portions of the pancreas, part of the left lobe of the liver adherent to or invaded by the cancer, and large segments of the transverse colon have all been removed in continuity with the entire stomach on numerous occasions. In the earlier years of gastric surgery, any one of these complications, i. e., the adherence of such organs to the stomach, would have constituted an excuse for classifying the cancer in that particular patient as irremovable.

B. DUODENUM AND PANCREAS

Successful operations for malignant tumors of the duodenum, in years

past, were limited to the rare occasions when a transduodenal resection of an early polypoid tumor of the ampulla of Vater could be done. All other cancers of the duodenum and pancreas were considered inoperable because surgical ingenuity had not devised a method of removing the duodenum and pancreas with re-establishment of biliary flow and gastro-intestinal continuity until Allen O. Whipple and his co-workers conceived of the principles now well established in the operation known as duodenopancreatectomy. Even with general employment of this operation, it is safe to assert that the great majority of patients with technically resectable cancers of the head of the pancreas and the duodenum are denied an opportunity for life because of the lack of surgical experience on the part of surgeons to whom they are entrusted, or the reluctance of these surgeons to undertake an operation of this magnitude. As an example of our own failure to think clearly, I would like to cite the following case history.

Case 4: C. F., a woman of 50 years, had hematuria due to a clear-celled papillary adenocarcinoma of the right kidney. The usual nephrectomy was done in the Memorial Hospital, from which she convalesced without complications. Several months later, she left for a vacation in Europe, and while there, her family noticed a progressively increasing jaundice. By the time she returned to the Memorial Hospital, she had become emaciated due to an extremely rapid weight loss, was vomiting incessantly, had become deeply jaundiced, and a mass could be felt in the right hypochondrium. Barium feeding and roentgen-ray studies revealed an obstruction in the second part of the duodenum. Because of the recent history of right nephrectomy and the location of the present mass, a presumptive diagnosis of recurrent renal cancer was made with secondary involvement of the liver, duodenum, and pancreas. The condition was deemed inoperable and laparotomy was therefore not attempted. The patient died in the hospital, and a postmortem examination was secured. There was no evidence of recurrence of the renal cancer. A papillary carcinoma of the ampulla of Vater was found, causing practically complete obstruction of the bile ducts and almost complete obstruction of the duodenum. There was no evidence of metastasis from this second cancer, and it would have been a technically easy feat to have removed it by the classical Whipple operation. In this instance, the diagnosis of inoperability was in error, due to a biased opinion based on the previous history of a recent cancer of the kidney, and the failure on our part to consider the symptoms and physical findings as typical of an ampullary cancer.

C. COLON

We now know that the colon may be removed in its entirety, as is done in those patients with multiple or diffuse polyposis of the bowel or in those with multiple colonic cancers. Many cancers of the colon, particularly of the papillary type which are commonly infected, are adherent to adjacent organs. This does not constitute a state of inoperability because in the majority of cases, these neighboring viscera may be removed safely with the colon. For example, there have been numerous instances in which we have resected a large segment of the colon, combined with hysterectomy in the female, or a wide segment of the pelvic colon with partial cystectomy in the male, or the splenic flexure with an adherent spleen. In one instance, a right hemicolectomy was done with a resection of two loops of adjacent ileum to include large nodes in the adjacent mesentery; the pathologic diagnosis was reticulum cell

lymphosarcoma. Multiple anastomoses were performed in a single-stage operation and the patient was living and well for eight years until she died of a heart attack. A cancer of the transverse colon with an external fistula of six months' duration was resected with a large segment of the abdominal wall without difficulty. There have been several cases in our series with the transverse colon adherent to the stomach, and in some instances, with perforation and fistula formation so that colectomy was combined with subtotal gastrectomy in order to remove the cancer in toto.

D. RECTUM

Many errors are made in diagnosing a rectal cancer as technically inoperable because of fixation as judged by digital examination of the cancer through the rectum. Many cancers which appear to be firmly adherent in the hollow of the sacrum or to the lateral wall of the pelvis when felt by combined recto-abdominal palpation can be successfully removed at the time of laparotomy. Unless the cancer is completely fixed to cause the so-called frozen pelvis, and providing the patient does not have evidence of distant metastases in the liver or in signal nodes, these patients profitably may be explored. This sometimes results in the happy discovery that the adherence of the cancer is a pseudo-fixation that can readily be relieved by dissection. Cancers of the rectum, because of their tendency to infection and extension through the wall of the bowel, become adherent to adjacent pelvic viscera such as the urinary bladder or the uterus. Under these circumstances, these organs should be removed in part or in whole, depending upon the extent and particular site of involvement. Three brief case histories are appended here to illustrate the plan of procedure under these conditions.

Case 1: K. D., a 71-year-old woman, had a bulky adenocarcinoma of the rectum filling almost the entire ampulla and invading the rectovaginal septum. It had perforated into the vagina, which was filled with a fungating sphacelate tumor. The entire perineum and perineal body were infiltrated by cancer. We performed an abdomino-perineal rectal resection associated with a vaginectomy. The vaginal mucosa overlying the base of the bladder was left intact, but the remainder of the vagina was removed with the rectum. Convalescence was uneventful. This same operation of rectal resection and vaginectomy, sometimes with an associated hysterectomy, has been done at least five or six times.

Case 2: B. K., a woman 56 years of age, had a carcinoma of the rectosigmoid. A previous supracervical hysterectomy had been performed. The cancer had become adherent to and invaded the urinary bladder. A superior segmental resection of the carcinoma was performed, together with a subtotal cystectomy. The operation was completed by an end-to-end anastomosis of colon and rectum. Convalescence was uneventful.

Case 3: M. S., a woman 54 years of age, was admitted to the hospital in a state of shock due to recent multiple hemorrhages which had been almost exsanguinating. A huge tumor was found to occupy the rectum, involving the rectovaginal septum, the posterior fornix and adherent to the cervix and uterine isthmus. A biopsy was reported as leiomyosarcoma. The terminal portion of the rectum was uninvolved by the tumor. An abdomino-perineal rectal resection was performed, together with a radical pan-hysterectomy and vaginectomy. The rectal sphincter was preserved, and the entire rectum was removed by reaming out the mucosa from the sphincter, after which the sigmoid

colon was brought down through the pelvis and hollow of the sacrum to protrude through the dilated sphincter. Healing occurred by primary union, and the patient was discharged from the hospital within two and one-half weeks. The function of the sphincter soon returned, and she was able to have normal bowel movements by rectum.

E. VAGINA

General surgeons and gastro-intestinal surgeons operating on cancers of the rectum have, on many occasions, performed a partial vaginectomy, together with an abdomino-perineal rectal resection for those rectal cancers that involve the rectovaginal septum. This has been an accepted mode of procedure. Gynecologists, on the other hand, and almost without exception, have been prone to classify all vaginal cancers as inoperable. The case of inoperability has even been listed on the patient's chart as due to invasion of the rectovaginal septum, with the statement that vaginectomy could not be done without entering the rectum. From the patient's point of view, a death from cancer of the vagina is just as bad as death from rectal cancer, and a permanent terminal abdominal colostomy for cancer of the vagina should be just as acceptable as it is for cancer of the rectum. On two occasions in which vaginal cancers were involving the posterior vaginal wall and posterior fornix, we have performed the operation of abdomino-perineal rectal resection with vaginectomy. If these vaginal cancers are infiltrating, and many of them are, there should be no hesitation in removing the rectum, even though it entails a permanent colostomy.

F. PROSTATE

The radical operation for cancer of the prostate as originated by Dr. Hugh Young has found some acceptance for those prostatic cancers that are removable. Total cystectomy for cancers of the urinary bladder is being done much more frequently in conjunction with bilateral uretero-sigmoidostomy. An example of the extension of radical surgery for cancer ordinarily classified as inoperable may be given in the following case report:

S. L., a Greek-American, 58 years of age, had been in excellent health without complaints until only two months prior to hospital admission. Since that time, he had had some frequency and urgency of urination, but the chief complaint was progressive constipation and later the passage of mucus and blood in his stools. At the time of admission, he had complete rectal obstruction with great abdominal distention. On digital examination, the ampullary portion of the rectum was completely obstructed by a firm mass, a biopsy of which revealed adenocarcinoma of undetermined histogenesis. The blood urea nitrogen was 87 mg. percent, and the patient was in a state of uremia. The situation was critical, but an immediate transverse colostomy was performed in order to relieve the intestinal obstruction. This was followed in a few days by a bilateral external ureterostomy by Dr. Archie Dean. After the blood urea nitrogen had returned to normal and the patient's condition had been greatly improved by blood transfusions and the institution of proper diet, a third operation was performed, which was of radical character. The terminal segments of the ureter, the entire urinary bladder, the prostate, the pelvic colon, the rectum, and the perineum were removed in continuity and entirely. The operation practically consisted of an exenteration of the true pelvis. So much peritoneum was removed with the specimen that the pelvic floor could not be reconstructed, so the principle of a Coffey dam with packing below was employed. The cancer was found to be primary in the prostate, and it practically replaced the entire organ.

The cancer had extended secondarily to involve the adjacent rectum and completely occlude it. It also infiltrated into the base of the urinary bladder and involved the entire bladder with bilateral obstruction of the ureteral orifices. The convalescence was protracted, due to the huge space left after ablation of these organs, but no serious complications occurred, and he was discharged from the hospital in good health.

G. TUMORS PRIMARY IN OR ADHERENT TO THE BONY PELVIS

The involvement of the os innominatum, with the exception of the iliac crest, by a primary malignant tumor of bone had in the past almost invariably been considered as inoperable. Furthermore, cancers primary on the lower extremities, such as synoviomas, malignant melanomas, and epitheliomas, after metastasis to the groin and extension into the iliac nodes with adherence, were deemed inoperable because of the extent of the disease. Primary malignant bone tumors of the pelvic bone and tumors in the region of the buttock, such as sarcomas of the soft somatic tissues that are adherent, and metastasizing melanomas and epitheliomas that involve the iliac nodes with adherence, are now being treated by such a radical procedure as hemipelvectomy, or the so-called interilio-abdominal amputation. We have performed a series of ten hemipelvectomies at the Memorial Hospital, based on these indications, without an operative death.

H. MALIGNANT TUMORS OF THE ORAL CAVITY AND ADJACENT SINUSES

The same principle of radical surgery is now being applied for the treatment of cancers that develop in the head and neck, particularly those involving the mucous membranes. Examples of the surgical treatment of cancers previously deemed inoperable are cited in the two following case reports.

Case 1: A. S., a 19-year-old boy, came to the Lendrim Tumor Clinic of the Paterson General Hospital with a huge osteochondrosarcoma involving the left maxillary antrum. The tumor had extended into the orbit with destruction of the orbital plate and caused protrusion of the eyeball with diplopia. It had eroded away the medial wall of the antrum and was fungating with obstruction into the left nasal chamber. It spread through the external wall with marked extrusion of the cheek. It had destroyed the floor of the antrum and the roof of the mouth and was perforating into the mouth, through the hard palate, and the left superior gingivo-buccal gutter. After bilateral ligation of the external carotid arteries, the classical Hautant-Monod exposure was obtained by incising through the philtrum of the upper lip and along the naso-malar fold and the margin of the left lower eyelid with retraction of the skin and subcutaneous flaps laterally. The entire left superior maxilla with the major portion of the roof of the mouth, the zygoma, the floor of the orbit, and the lateral aspect of the nasal chamber were then surgically completely removed. The tumor proved to be an osteochondrosarcoma. His convalescence was uncomplicated, and the defect in the roof of his mouth was corrected by an obturator attached to a superior dental plate. The floor of the orbit was replaced by a temporal muscle transplant to serve as a hammock. The eyeball resumed its normal position and vision was undisturbed. Fourteen years have elapsed since the operation. The patient is living and well, has graduated from college, and is a religious teacher.

Case 2: A. T., a Hindu, came from Bombay in a very weakened condition due to extreme pain and inanition secondary to an advanced cancer of the tongue. This carcinoma involved the entire left side of the tongue, extending from the tip to the vallecula, and infiltrating deeply to the middle of the tongue. The carcinoma involved the entire left side of the floor of the mouth and was adherent to and invading the horizontal

ramus of the left mandible. It extended onto the region of the left tonsil and tonsillar pillars and caused trismus so great that the jaw could not be opened. Firm lymph nodes in the left submaxillary region were replaced by metastatic carcinoma and were inseparably adherent to the under surface of the mandibular ramus. Other lymph nodes were present in the left digastric group. He was admitted to the Doctors Hospital, where under intratracheal anesthesia, the left lip was bisected and the skin flaps turned widely back in continuity with a Bastianelli incision for radical neck dissection. The dissection of the left neck was accompanied by ligation of the external carotid artery. The lymph nodes in the left submaxillary region were so firmly adherent to the mandible and to the underlying muscles that all of the structures of the submaxillary triangle were removed, together with the hyoid bone to which the carcinomatous nodes were adherent. The mandible was severed through the mental process. The left side of the mandible, together with the entire floor of the mouth and the left lateral two-thirds of the tongue, was then completely severed in the anterior posterior direction. The mandible was then disarticulated at the temporomandibular joint, and the base of the tongue, together with the tonsil and tonsillar pillars and the left side of the oral pharynx, were dissected down to the pterygoid fossa. The mucous membrane of the left cheek along the gingivo-buccal gutter was then approximated to the lateral aspect of the severed tongue, and the skin flaps were also approximated by a plastic procedure. The operation was terminated by a tracheostomy. The patient was out of bed 24 hours after the operation and was fed for two weeks by means of a nasal catheter. At the time the tracheostomy tube was removed, he was able to swallow food by mouth; the mouth was fairly well healed; and his voice was quite satisfactory except for lingual sounds.

SUCCESSFUL SECONDARY OPERATIONS FOR CANCER

The surgeon is frequently confronted with patients and their relatives who relate the story of exploratory laparotomy followed by a pronouncement of inoperability and, in consequence, incurability of the cancer. They usually importune the next surgeon seen, and perhaps many others, to intervene again, not being willing to accept the opinion and judgment of the initial surgeon, who had an opportunity to study the extent of the cancer at the time of laparotomy. Physical examination of such patients, after their discharge from other hospitals, may often permit the later surgical consultant to agree in the obvious diagnosis of inoperability. However, in the absence of physical signs of inoperability, one is sometimes justified in sending a note of inquiry to the surgeon, requesting a copy of the operative findings. If the reasons for not resecting the cancer were given as distant metastases, for example, in the liver, or diffuse peritoneal carcinosis, then the indications of inoperability must be considered absolute. But if the operative findings are listed, indicating that the decision not to remove the cancer was based on technical difficulties, there may exist a suitable excuse for a second attempt at removal. It may seem presumptuous to attempt an operation in the face of a previous failure by one who has had an opportunity to inspect the cancer and its extent at the time of laparotomy, but in some of the following case reports, the wisdom of this decision seems apparent. Such secondary operations should be taken with a full understanding by the family that it might not be possible to complete the operation successfully.

1. *Stomach. Interval before Secondary Resection—27 months*—R. B., a 39 year-old man, came to the Gastric Clinic of the Memorial Hospital with the story that two years

and three months before, he had been subjected to a laparotomy for a gastric cancer, which was found to be inoperable. The story seemed incredible because, in our experience, the average patient with inoperable gastric cancer is dead within a year after the date of the diagnosis. A letter was dispatched to the hospital for a loan of the slide of the biopsy. The slide revealed an adenocarcinoma, and the date of the biopsy was two years and three months previous, agreeing with the patient's statement. The surgeon's report classified the cancer as inoperable because it originated in the fundus of the stomach and was extending into the esophagus above the level of the diaphragm. Because careful physical examination did not reveal any evidence of distant dissemination of the cancer and because the patient seemed to be in good health, he was accepted for treatment in the Clinic. Gastro-intestinal roentgenogram studies revealed a huge tumor occupying the fundus and cardiac end of the stomach with extension for several centimeters into the esophagus well above the level of the diaphragm. A preliminary laparotomy was done for purposes of exploration. There were no metastases in the liver; the tumor although bulky was movable; and it was therefore possible to remove it by the combined thoracic and abdominal approach. The exploratory operation was terminated by a jejunostomy for feeding purposes. Two weeks later, a thoracotomy was performed and the diaphragm severed. The distal segment of the esophagus was removed and the major portion of the stomach. There was not sufficient stomach left for esophago-gastrostomy. Since the remnant of esophagus was high under the aortic arch, one could not bring up a loop of jejunum to construct an intra-thoracic esophago-jejunostomy, particularly because a jejunostomy had been performed, and the operation had to be completed quickly. The esophagus was then brought out through the neck and onto the chest wall to construct an anterior thoracic esophagostomy. At a later date, the remnant of the stomach was brought to the anterior wall for a gastrostomy opening. The patient convalesced from these operations without complications. The significance of this case record is that it was still possible, by the transthoracic approach, successfully to resect the lower portion of the esophagus and the major part of the stomach for a cancer which had been diagnosed as inoperable in another hospital two years and three months prior to this date.

2. *Stomach. Interval Before Secondary Resection—3 months*—J. Z., a 58-year-old janitor, was operated on at the Memorial Hospital for cancer involving the distal sement of the stomach. Because the cancer had perforated through the serosa and because of its fixation to the pancreas, it was classified as inoperable and a gastro-jejunostomy was performed. When the attending surgeon left for a protracted European vacation three months later, the resident surgeon who had participated in the operation and disagreed in the opinion of inoperability, readmitted this clinic patient and then performed a gastric resection, removing the distal segment of the stomach below the site of the original gastro-jejunostomy. This patient is now living and well 16 years after the gastric resection. The gastric resection was done three months after the attending surgeon had classified the cancer as inoperable.

3. *Cecum. Interval Before Secondary Resection—9 months*—R. K., a man 42 years of age, had a laparotomy nine months before for cancer of the cecum. The cancer was diagnosed as inoperable because of apparent metastases involving lymph nodes in the mesocolon; these lymph nodes were said to be quite large and firm, but none was removed for microscopical study. The surgeon also observed numerous white nodules on the peritoneum in the mesentery of the small bowel and adjacent to the cecum and large intestine; these were interpreted as representing nodules of metastatic cancer. No microscopical study or confirmation of the diagnosis was made. Inasmuch as the patient, nine months later, did not have ascites nor an enlarged liver and was not greatly worse except for a progressive anemia, he was brought to New York City. At the Memorial Hospital, a second laparotomy was performed, and it was found possible to perform a right hemicolectomy with an anastomosis between the terminal ileum and transverse colon. The white peritoneal nodules previously described were no longer apparent and the enlarged

lymph nodes had subsided, which would lead one to infer that they were involved by inflammatory lymphadenitis, rather than by metastatic cancer.

4. *Duodenum. Interval Before Secondary Resection—7 months*—S. H., a young Naval officer, vomited a huge quantity of blood while in the Pacific Zone. A diagnosis of duodenal ulcer was made, and he was placed on a hospital ship and later returned to the United States. Several episodes of hematemesis occurred. Roentgen-ray studies were made on two occasions with a diagnosis of duodenal ulcer. Finally, four months after the onset of symptoms, and because of the occurrence of jaundice, a laparotomy was performed. A tumor was palpated in the region of the head of the pancreas, and a diagnosis of inoperable cancer was made; the operation was terminated by a cholecystojejunostomy.

Seven months after this operation had been performed, during which time the patient had not been informed as to the character of his illness, he was admitted to the Memorial Hospital. The early roentgen-ray films were obtained and they clearly showed the presence of a tumor in the second part of the duodenum. The diagnosis of carcinoma of the ampulla of Vater was made and a second laparotomy advised. After exploration, the classical pancreaticoduodenectomy was performed. The cholecystojejunostomy was left intact, but the common bile duct was also used to perform a choledochojejunostomy. The distal end of the severed stomach was implanted in the descending jejunal loop. The patient had an uneventful convalescence. The tumor proved to be a papillary adenocarcinoma of the ampulla of Vater.

5. *Duodenum. Interval Before Secondary Resection—30 months*—J. C., a man 45 years of age, came to the Memorial Hospital two and one-half years after he had been operated upon in another institution where a diagnosis of inoperable cancer of the pancreas was made. At the time of the first laparotomy, a cholecystgastrostomy was done. This relieved his jaundice, and he was in comparative comfort for more than a year. The cholecystgastrostomy stoma apparently did not function well, so after a second laparotomy a cholecystojejunostomy was done. One year later, due to obstruction of the duodenum by cancer, a third laparotomy was performed, at which time a gastro-jejunostomy was done. At this last operation the surgeon, who was not the one previously engaged, made a thorough exploration of the abdomen and observed that the cancer had not metastasized to the liver and that it was movable, though bulky. As a result of his findings, he advocated a fourth laparotomy which was done on the Gastric Service of the Memorial Hospital. We were able to perform the usual pancreaticoduodenectomy and completed the operation by imbedding the common bile duct in the jejunum for a choledochojejunostomy. The carcinoma was an infiltrating cancer involving the ampulla of Vater and the head of the pancreas. Convalescence was uneventful. The patient is now living and well two years after the successful resection. The unusual feature of this case report lies in the fact that the first actual attempt at resection of this cancer was on the occasion of the fourth laparotomy.

6. *Rectum. Interval Before Secondary Resection—4 months*—A. W., a 41-year-old woman, entered the hospital with a large carcinoma of the rectum which appeared moderately fixed on recto-abdominal palpation. Four months before, a laparotomy had been performed at another hospital, at which time the cancer was considered inoperable because of local technical difficulties. The operative notes at that time indicated that there was no evidence of distant dissemination and no evidence of metastasis in the liver. Two months later, the patient entered another hospital where a second laparotomy was performed by another surgeon. He also classified the rectal cancer as inoperable and performed a simple loop colostomy. When we examined the patient, we found a functioning sigmoid colostomy. There was a large carcinoma completely encircling the lumen of the bowel in the upper rectal ampulla; it was moderately fixed to the pelvic wall. As there was no palpable enlargement of the liver, we decided to attempt a resection. Accordingly, a laparotomy was done and it was found possible to perform an abdomino-perineal rectal resection. The patient convalesced from this operation without complications. The state-

ments of the two previous surgeons concerning the inoperability of the cancer were based, therefore, solely on technical difficulties, rather than on the actual stage of the disease.

7. *Retroperitoneal Sarcoma. Interval Before Secondary Resection—6 weeks*—R. L., a 5 months old infant, was admitted to the Children's Ward of the Memorial Hospital with a huge tumor in the left iliac quadrant. Six weeks before, an operation had been performed in another institution, at which time the location of the tumor was thought to be retroperitoneal and beneath the mesentery of the colon. It was considered inoperable and a biopsy only was obtained, which was reported as a sarcoma. We subjected the child to a laparotomy and after careful dissection, were able to remove the retroperitoneal sarcoma and preserve the integrity of the overlying intestines. It was diagnosed as a rhabdomyosarcoma of embryonal type. There was no evidence of metastasis of this sarcoma. Again, in this instance, the diagnosis of inoperability was based solely on technical difficulty, and the dissection was not attempted because of this fact, although it was obvious that the child would die of the sarcoma.

SUMMARY

The definition of inoperability of cancer has an important influence on end results. The point of view of the surgeon plays a significant role in determining whether or not a given patient should be subjected to operation and attempt at surgical removal of the cancer. A distinction should be made between *absolute* inoperability due to distant dissemination of the cancer and obvious incurability, and *relative* inoperability due to local technical difficulties. No surgeon should perform an exploratory operation unless he is qualified to proceed with the actual removal of the tumor if encountered. Excisional surgery should be available for cancer patients of advanced age if they can be prepared for such an ordeal, as old age alone is not a sufficient excuse to deny these patients the only opportunity to overcome an otherwise fatal disease. The condition of the patient may present seemingly serious hazards from the surgeon's viewpoint, but with the current improvement in preoperative and postoperative management, the dangers are often reduced to the point where major surgical procedures may be safely performed. The stage and extent of the cancer complicate the judgment of the surgeon, but if the cancer is removed whenever technically possible, occasional cures are surprisingly obtained. Palliative resections of the stomach, colon, and rectum afford a great deal of relief to many patients even though small metastatic foci are detected in the liver. Involvement of multiple organs by cancer has been given as a reason for inoperability, but one should attempt by every means possible to remove such cancers which are adherent to any adjacent structures or viscera that may be sacrificed by excision in continuity with the organ involved. Some patients who have had exploratory laparotomy for cancer with abandonment of the operation and pronouncement of incurability are entitled to another chance or effort by a different surgeon if the former surgeon classified the cancer as inoperable because of technical difficulties. Case reports are inserted to illustrate the arguments throughout this thesis.

THE SURGICAL TREATMENT OF THE INFANTILE TYPE OF COARCTATION OF THE AORTA

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COARCTATION OF THE AORTA may be divided into two types according to the classification of Bonnet.[1] In the *infantile type* there is an elongated narrowing of the aorta at the isthmus while in the *adult type* there is an abrupt constriction at or near the ductus arteriosus. Maude Abbott[2] found records of 237 cases of coarctation of the aorta which came to autopsy, of which 155 were of the adult type and 82 were of the infantile type. She found that the infantile type was frequently associated with other congenital anomalies which contributed to the early death of the patient. In a later report she[3] noted that in 200 cases of the adult type which came to autopsy, the associated hypertension was the chief cause of death. The average age was 33 years. Of these, 39 died as the result of spontaneous rupture of the aorta or heart, 26 had cerebrovascular accidents, and 67 died of myocardial failure. Thus 66 per cent died at this early age as the result of the associated hypertension. This would seem to constitute sufficient cause for attempting to correct the congenital defect by surgical means.

The first operation performed for coarctation of the aorta was done by Crafoord[4] of Stockholm on October 19, 1944. He reported two successful operations on the adult type in which the constricted area was excised and the two ends of the aorta sufficiently mobilized to bring them together and do an end-to-end anastomosis. The Carrel suture technic was used. By June 1946 Crafoord[5] had operated upon seven patients of the adult type and was able to excise the short segment and do an end-to-end anastomosis in all of them.

Blalock and Park[6] and Gross and Hufnagel[7] had previously reported experimental work in dogs concerning this problem. Blalock had shown that the left subclavian artery might be brought down and anastomosed to the side of the aorta below the coarctation. Gross had shown that a segment of the dog's aorta could be excised and an end-to-end anastomosis done.

Gross[8] operated upon his first patient a short time after Crafoord and Nylin[4] and used the continuous everting mattress suture which he had used in experimental animals. By June 8, 1947 he[9] had operated upon 23 patients with only two deaths. The anastomosis was completed in 20 of the patients. There was so much inflammatory change present in one patient that the aorta could not be safely mobilized. The remaining two patients had lesions of the

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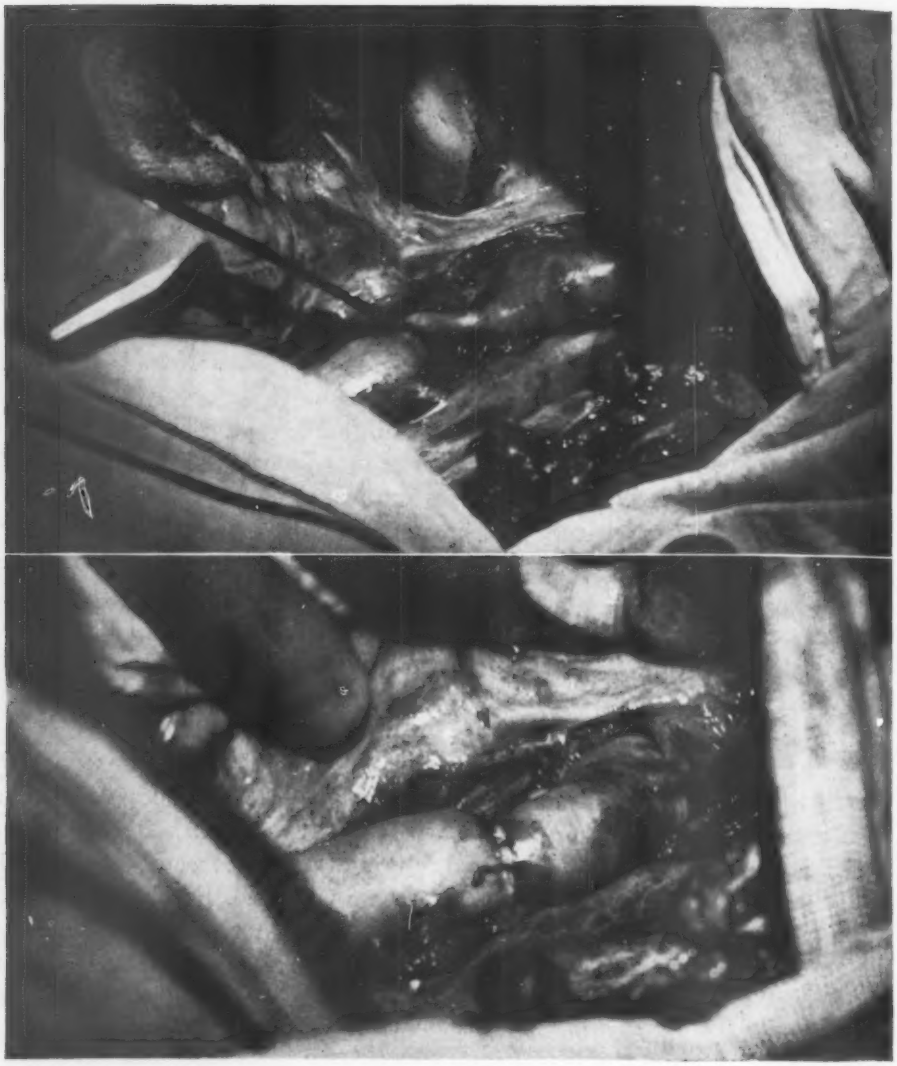
A



B

FIG. 1.—(A) Case 1. The infantile type of coarctative of the aorta. The stenotic area was long and the lumen of the vessel was completely obliterated. It was estimated 4.0 to 5.0 cm. of aorta would have to be excised preparatory to an anastomosis. Note the large first intercostal artery.

(B) The large left subclavian artery was divided, rotated downward and sutured to the end of the descending aorta.

infantile type, with such long areas of constriction that it would have been impossible to bring the ends of the aorta together had the constricted areas been resected. Gross considered these two patients inoperable. As of his last report Crafoord[5] had encountered none of the infantile type of coarctation.

We have recently operated upon three patients with coarctation of the aorta of the infantile type. In all three instances the constricted area extended over a distance of several centimeters. It was obviously impossible to perform the type of operation used by Crafoord or Gross. However, it seemed worth while to turn the left subclavian artery down to bridge the defect. In two patients the end of the subclavian artery was anastomosed to the upper end of the descending aorta after the area of the defect had been excised. In the third patient the operation had to be abandoned because of the friability of the vessels due to atheromatous changes.

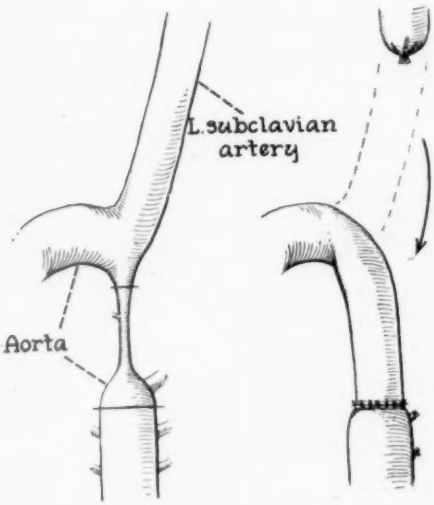


FIG. 1.—(C) A diagram of the procedure. The anastomosis was done, with a continuous everting mattress suture and with a few reinforcing interrupted sutures.

Case No. 1: V.B., a 13-year-old negro boy, was first seen by Doctor Rachel Ash at the Children's Hospital in July 1942, complaining of dyspnea and precordial pain on exertion. He had a blood pressure of 150/110 and a soft blowing systolic murmur in the first and second interspaces to the left of the sternum. On roentgen-ray examination a small aortic knob and indentation of the inferior borders of several ribs were seen. The femoral and dorsalis pedis pulses were barely palpable. A diagnosis of coarctation of the aorta was made. In subsequent follow-up studies the weak pulses in the lower extremities disappeared completely.

Upon admission to the Hospital of the University of Pennsylvania on January 6, 1947, the boy appeared to be normal mentally and physically except for the above findings. He was symptom free except upon strenuous exertion. He weighed 90 pounds. The blood pressure was 160/110 in both arms. It was unobtainable in the legs. No pulse was palpable in the abdomen or lower extremities. The cold perssor test showed a rise to 220/150 in 30 seconds. Studies of blood flow by the ballistocardiograph and studies of renal blood flow were made pre- and postoperatively*.

Studies of renal blood flow showed a significant increase in Case No. 1 with an increase of a magnitude not great enough to be significant in Case No. 2.

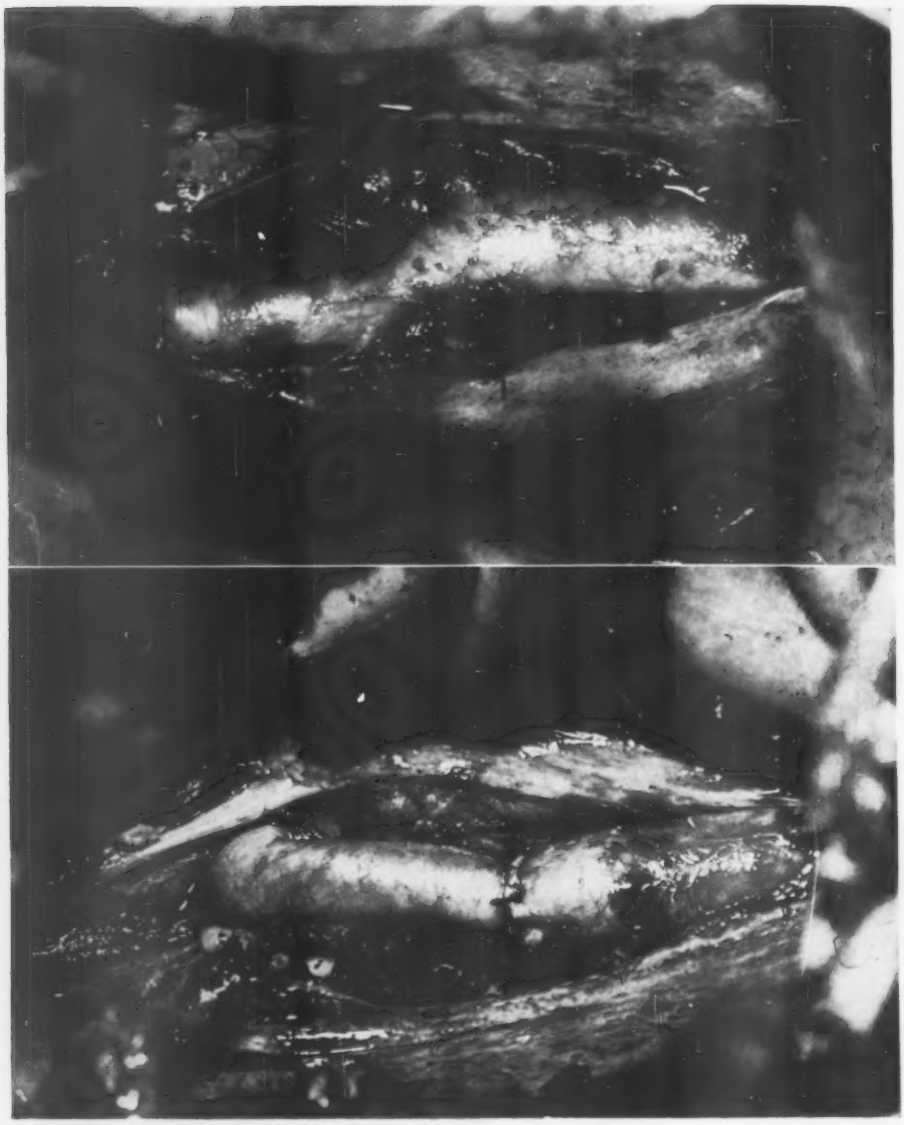
EFFECTIVE RENAL BLOOD FLOW

	January 16	January 29	May 16
Case No. 1	880 cc./min.	1130 cc./min.	1080 cc./min.
	February 19	April 26	
Case No. 2	1120 cc./min.	1200 cc./min.	

The blood flow was calculated from para-amino hippurate clearance and hematocrit readings. These tests were done by Doctors J. K. Clark, G. J. Gislason and H. G. Barker and will be reported in detail elsewhere.

* Studies of blood flow by the ballistocardiograph in Cases 1 and 2 indicated an increase in blood flow in both patients following operation.

A



B

FIG. 2.—(A) Case 2: In this patient there was a small lumen in the coarctation, but the area of significant decrease in diameter was about 4.0 to 5.0 cm. long.
(B) The left subclavian artery was rotated downward and sutured to the end of the descending aorta.

The patient was operated upon on January 17, 1947 under endotracheal cyclopropane anesthesia. With the patient on his right side the left fifth rib and short segments of the fourth and sixth ribs were resected. The coarctation of the aorta was recognized as being infantile in type with a stenotic area 4.0 to 5.0 centimeters in length, as shown in the accompanying photograph and diagram. The aorta was freely mobilized by dividing

5 intercostal arteries, but it was obvious that the ends of the aorta could not be brought together for an anastomosis if the stenosed segment were excised. The left subclavian artery was found to be quite large. It seemed reasonable, therefore, to divide the subclavian artery, rotate it downward and anastomose it to the descending aorta as Blalock and Park[6] had done experimentally in dogs. The aorta was ligated and divided. Its lumen was found to have been completely obliterated at the site of greatest narrowing. Since the subclavian artery was almost as large as the descending aorta an end-to-end anastomosis was done without difficulty, using the everting mattress suture as described by Cross and Hufnagel.[7] Crafoord clamps covered with white shoe strings were used to occlude the arota. The clamps were gradually removed over a period of three minutes with no change in the patient's condition. It was immediately possible to feel bounding pulses in both feet. The patient's postoperative course was uneventful. He was allowed to be out of bed on the first postoperative day and began to walk on the fifth postoperative day. The blood pressure came down slowly. Between the tenth and twentieth post-operative days the blood pressure in the right arm averaged 120/80 and in the legs 110/70. The child was discharged on the twenty-first day feeling entirely well.

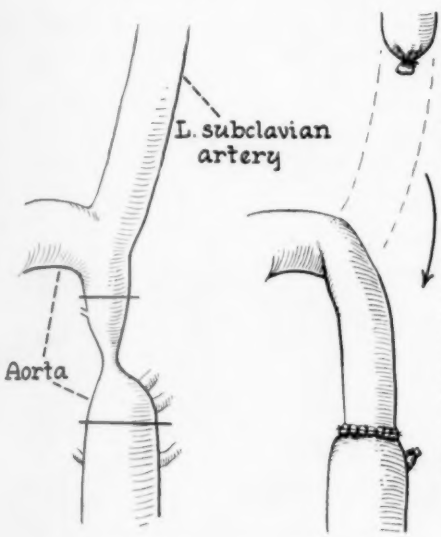


FIG. 2.—(C) A continuous everting mattress suture was used, but because of the difference in the size of the vessels, several interrupted sutures were placed at the site of buckling.

He was re-examined on the thirteenth of November 1947, 10 months after operation. He had gained 22 pounds in weight and 3.5 inches in height since operation. The blood pressure in the right arm was 115/70 and in the legs was 105/65. He had good pulses in both feet. A soft blowing systolic murmur was still present to the left of the sternum in the second interspace. The patient stated that he felt perfectly well and had no symptoms of any sort during strenuous exercise.

Case No. 2: C. I., a 17 year old boy, was rejected for military service in April 1946 because of high blood pressure. His only complaint was that when participating in high school track he could not run the mile even after much practice. He was first studied in the Cardiac Clinic and then admitted to the Hospital of the University of Pennsylvania on the sixteenth of February 1947. He weighed 120 pounds and appeared to be in good condition. The blood pressure in his arms was 160/90 and was unobtainable in his legs. No pulses were palpable in the lower extremities. A harsh mid systolic murmur was heard best in the second and third interspaces to the left of the sternum and also along the vertebral border of the left scapula. By fluoroscopy the heart was normal in size, and the aortic knob was not visible. There was notching of the fourth and fifth ribs. A diagnosis of coarctation of the aorta was made. Studies of blood flow by the ballistocardiograph and studies of the renal blood flow were made before and after operation.* During the cold pressor test the blood pressure did not rise appreciably. During the sodium amytal test the blood pressure fell to 130/90.

The patient was operated upon on February 26, 1947. The same approach was used as in Case No. 1. The coarctation was found to be infantile in type (see photograph and diagram). It was not complete but extended over a distance of 4.5 to 5.0 centimeters.

*Refer to footnote on page 1121.

An effort was made to preserve the intercostal arteries as suggested by Crafoord,[5] but in so doing one was torn and considerable difficulty was encountered in controlling the hemorrhage. Finally 6 arteries were divided in order adequately to mobilize the aorta. As may be seen by the photographs, the subclavian artery was not as large in proportion to the aorta as in the first patient, but it was divided and the proximal end rotated downward and anastamosed to the end of the aorta. When the clamps were removed, a moderate pulse could be felt immediately in both lower extremities. The postoperative course was uneventful. The pulses in the legs seemed weaker 2 or 3 days after operation than on the day of operation. After 3 weeks the blood pressure had changed from an average of 160/90 to 160/70. The patient was discharged symptom free on the twenty-second day.

Upon readmission on the twenty-fourth of April 1947 the pulses in the lower extremities seemed stronger than upon discharge. The blood pressure in the right arm was 160/70 and in the legs was 120/95. The patient is still symptom free. He has no drop in his systolic pressure, but the diastolic pressure in his upper extremity has returned to normal.

FIG. 3.—Case 3. The lumen of his aorta was completely obliterated at the point of greatest narrowing. The length of the stenosed area, which was smaller than the left subclavian artery, was measured to be 5.0 centimeters.

Case No. 3: S. S., a 20-year-old boy, was rejected by the army because of hypertension. For the last 2 or 3 years he had been having increasing dyspnea upon exertion. Finally this became so severe that he could not hold a job. He weighed 120 pounds. His blood pressure varied between 220/120 and 260/120. Roentgen-ray examination showed an absence of the aortic knob and indentation of the inferior border of several ribs. No pulses were palpable in the lower extremities.

A diagnosis of coarctation of the aorta was made and operation advised. The operation was performed by the same approach as in the two previous cases. The coarctation was found to be infantile in type. It was 5.0 centimeters in length by actual measurement. It was decided to attempt the same procedure as used in the first 2 cases. We were first aware that we might be in trouble when we divided the subclavian artery and found the inside yellow with atheromatous plaques; and when we attempted ligation of the coarcted area of the aorta, the ligature cut through. The subclavian artery was

not as long as in the 2 previous patients. It appeared that some slight tension was present as the two vessels were approximated. Although the tension seemed very mild, the subclavian artery ruptured at the site of an atheromatous plaque fairly close to the aorta. When a clamp was applied across the subclavian artery to control the massive hemorrhage, it cut partly through the vessel wall. A heavy silk ligature placed proximal to the clamp also cut partly through the wall, but a No. 2 chromic catgut ligature placed further proximally controlled the bleeding satisfactorily at the time. A suture ligature was placed distal to it. The operation was abandoned. The blood pressure had fallen during the operation, but 12 hours after operation his blood pressure reached the preoperative level of 260/120, and he suddenly succumbed. Autopsy showed that the subclavian artery had torn through at the site of the most proximal ligature. The entire aorta and the great vessels above the coarctation were extensively covered with atheromatous plaques, and all were very friable.

COMMENT

In the infantile type of coarctation of the aorta excision of the area and end-to-end anastomosis will probably never be feasible. Gross in two instances has considered this type inoperable. If the subclavian artery is to be used for the anastomosis, as was done here, the question will always arise as to whether the blood flow is materially increased by the procedure. In Case No. 1 no blood was going through the coarctation, but five intercostals were divided. It is evident, however, that this patient was improved. A bounding pulse was present in his lower extremities, and the blood pressure in the upper extremities returned to normal. In Case No. 2, however, some blood was going through the coarctation. Not only this was sacrificed, but also 6 intercostal vessels. It is, of course, questionable whether the subclavian artery delivered more blood flow to the descending aorta than was sacrificed. The presence of palpable pulses in the lower extremities postoperatively suggests some increase in blood flow. That the increase was not adequate is indicated by the failure of the systolic blood pressure to return to normal although there was some fall in the diastolic pressure.

Although Gross[9] had previously pointed out the hazard of operating upon patients in the older age group, we felt that we were justified in attempting Case No. 3 at the age of 20 inasmuch as Crafoord[5] had been successful in several patients of this age group. The difficulty here lay in not being able to recognize until it was too late that the vessels were too friable to be worked with. Perhaps the preoperative blood pressure of 260/120 should have been sufficient warning to us. With the chest open and the vessels exposed it was still impossible for us to ascertain the true condition of the vessel walls until after the vessel had been cut across and the atheromatous changes visualized. If this information could be obtained without actually opening the vessel, the difficulties encountered in Case No. 3 might be avoided by abandoning the operation before sacrificing any of the blood flow already present.

The problem arises as to the age to elect to operate upon the patient with coarctation of the aorta. If it is done too early, there is some question as to whether the site of anastomosis will grow with the patient. If it is done too

late, the vessel wall may be so friable as to make the suture hazardous. It would seem that 12 to 14 years of age would be the most satisfactory time.

SUMMARY

1. Three patients (age 13, 17 and 20) with the infantile type of coarctation of the aorta were operated upon.

2. In two patients the subclavian artery was divided and rotated downward to bridge the defect by an end-to-end anastomosis with the descending aorta. In a third patient the operation had to be abandoned because of the atheromatous condition of the vessel walls, and the patient succumbed from hemorrhage in the immediate postoperative period.

3. The first patient obtained a good result with the blood pressure in the upper extremities returning to normal. The second patient's systolic blood pressure did not fall although the diastolic pressure returned to normal.

4. We believe that the use of the subclavian artery to bridge the gap in the infantile type of coarctation of the aorta is worthy of further trial in selected cases.

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BATTLE WOUNDS AND INJURIES OF THE HEART AND PERICARDIUM

Experiences in Forward Hospitals

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SEVENTY-FIVE PATIENTS with wounds of the heart or pericardium were cared for by surgeons of the Second Auxiliary Surgical Group in Field and Evacuation hospitals. This is an incidence of 3.3 per cent in the group of patients with thoracic and thoracic-abdominal injuries (total of 2,267 cases) whose initial surgery was performed by surgeons of the unit. Fifty-seven per cent (43 cases) occurred in patients whose wounds involved the thorax only. One of the 75 injuries was due to a self-inflicted stab wound and the remainder were battle-incurred. Fifty-three soldiers were wounded by shell fragments and 21 by small arms fire. There were 18 examples of wounds of the pericardium only and 57 patients had traumatic lesions of the heart itself.

The following report is based on the writer's personal experience and on a careful review of all additional records in the files of the unit. This was supplemented in most instances by personal contact with each operating surgeon.

DIAGNOSIS

It was not always easy to diagnose cardiac wounds and injuries in forward hospitals. Electrocardiograms were not available and roentgenograms were limited for the most part to frontal and lateral films. Fluoroscopy was used to some extent but could have been employed more frequently. In slightly more than 50 per cent of all cases the actual cardiac wound was undiagnosed prior to commencing surgery. The thorax was opened in the majority of these because of probable thoracic-abdominal involvement, or for the debridement of large sucking wounds. In seven cases, suspected intrathoracic hemorrhage prompted exploration. In three cases, the presence of a foreign body in the mediastinum was an indication. In 15 cases (including two patients who died in the shock ward), the cardiac wound was discovered at autopsy.

In confirming the presence of cardiac injury, one finding alone is seldom conclusive (Table I).

Frequently a cardiac wound may be suspected by thorough physical examination and accurate localization of external wounds. Plotting of the missile track often can be done when examination is combined with roentgen studies showing the location of foreign bodies and the site of fractured ribs. When the foreign body is in, or in the region of, the heart, it may appear fuzzy or double-contoured. When localizing missiles within the cardiac shadow, heavy penetration must be used either by means of "bone technic" or the Potter-Bucky diaphragm. Often a missile will be completely over-

looked in a thoracic film of usual exposure. Fluoroscopy may be used frequently to study the motion of the missile and whether or not it is included within the cardiac shadow in all projections. The size and shape of the cardiac shadow may be altered and has been described as "water-bottle," fuzzy, or enlarged. The latter interpretation may be subject to question since the pericardium usually does not stretch appreciably when intrapericardial fluid first develops. In two cases where the cardiac outline was blurred or fuzzy on the roentgen film, operation disclosed considerable hemorrhage into the pericardial membrane and the areolar tissue of the lower mediastinum.

Signs of anoxia may be present in patients with cardiac wounds. Before attributing these signs to a cardiac lesion care must be exercised in eliminating other causes of oxygen want, such as extensive peritoneal contamination,

TABLE I.—*Signs and Symptoms Suggesting Cardiac Lesions* *

Suspicion from course of missile	22
Roentgen evidence	
Foreign body in region of heart (4, labeled fuzzy or double contoured)	8
Foreign body suspected in region of heart, not proved	2
Alterations in size or shape of cardiac shadow	5
Symptoms due to anoxia	
Dyspnea	6
Necessity for early and continuous oxygen administration	6
Mental confusion or semi-stupor	5
Cyanosis	3
Signs suggestive of cardiac dysfunction	
Persisting tachycardia (120 or above)	8
Arrhythmia (transient fibrillation, 1; extra systoles, 7)	8
Bradycardia (below 65)	2
Apical systolic murmur	2
Friction rub, precordial	2
Paradoxical pulse	1
Nausea and vomiting	1
Cardiac tamponade	5
(Recognized clinically....3)	
(Suspected, but untreated. 1)	
(Unsuspected.....1)	

* This table is a compilation of the number of *times* that each sign or symptom was noted in proven cardiac cases. In a few instances the findings were noted on the records but their significance was not appreciated until after the cardiac lesions had been discovered at operation or at autopsy.

multiple wounds, hemorrhage, and large hemothorax or pressure pneumothorax. There remain cases in which peritoneal contamination can be ruled out and in which hemothorax and hemorrhage have been corrected by thoracentesis and transfusion. In these, there may be persisting dyspnea, cyanosis, or mental confusion which are out of proportion either to the visible thoracic damage or to the signs of continuing hemorrhage. In such instances a cardiac lesion may be assumed to be the basis for the continuing anoxia.

Direct evidence of cardiac dysfunction may be encountered. It is certain that more frequent cardiac examinations would have increased the number of

positive findings. Thus, three medical officers made all eight observations of arrhythmia. As with anoxia, other causes of tachycardia must be eliminated before it can be assumed that the continuing rapid pulse is of intrinsically cardiac origin. A soft systolic apical murmur is an exceptional finding.[1] The one example of paradoxical pulse was noted in a patient with severe myocardial contusion who died in the shock ward. Friction rubs were heard preoperatively in but two patients. In both, operation had been delayed and the rub became audible 24 hours after injury. Since a friction rub or splash was noted in eight additional cases postoperatively, it is evident that a certain time-interval is necessary for this sign to appear.

Persistent nausea with vomiting was seen during the preoperative period in one patient. Such a finding is rare in uncomplicated thoracic wounds and in the instance cited, it was possibly attributable to the cardiac wound.

TABLE II.—*Type of Cardiac Wound, 57 Cases.*

Anatomic Portion Involved	Lesion					
	Contusion	Pure Laceration	Laceration and Contusion	Perforated Chamber	Embolism to Heart	Total
Ventricle						
Left.....	7	7	5	7	0	26
Right.....	5	2	2	3	2	14
Both.....	3	0	2	0	0	5
Auricle						
Left.....	0	0	0	2	0	2
Right.....	1	1	0	7	0	9
Right auricle and right ventricle	0	0	1	0	0	1
Total lesions.	16	10	10	19	2	57
Deaths						
Total	11	1	5	9	1	27
Due to heart (rate).....	6 (37.5%)	1 (10%)	4 (40%)	8 (42.1%)	1 (50%)	20 (35.1%)

In comparison to the great frequency with which it is noted in civilian cardiac injuries, tamponade was an unusual finding in war wounds of the heart: the missiles were larger and, frequently, wide pericardial lacerations usually allowed ample drainage into the pleural cavity. Tamponade always must be kept in mind because of its lethal potentialities. The blood often comes from a cardiac chamber, but it may also come from a severed coronary branch, from a vessel in the pericardium, or from the myocardium itself. Death occurred twice due to unrecognized tamponade although in one patient, with a severe thoracico-abdominal wound, it was suspected. In this instance exploratory puncture was not successful because all the blood in the pericardium had become clotted. In the three cases where tamponade was recognized, the diagnosis was based on the findings of distended neck veins, muffled heart sounds, and a "water-bottle" shape of the cardiac shadow. Lowered

pulse pressures were not recorded in these three cases. Fluoroscopy could have been used in determining whether or not pulsation was decreased or absent. Hemopericardium of from 50 to 150 cc. was noted in five additional cases at operation. In none had there been clinical evidence of increased intrapericardial pressure.

A precordial crunch or click synchronous with heartbeat and associated with mediastinal emphysema was heard occasionally. This sign was *not* indicative of cardiac trauma.

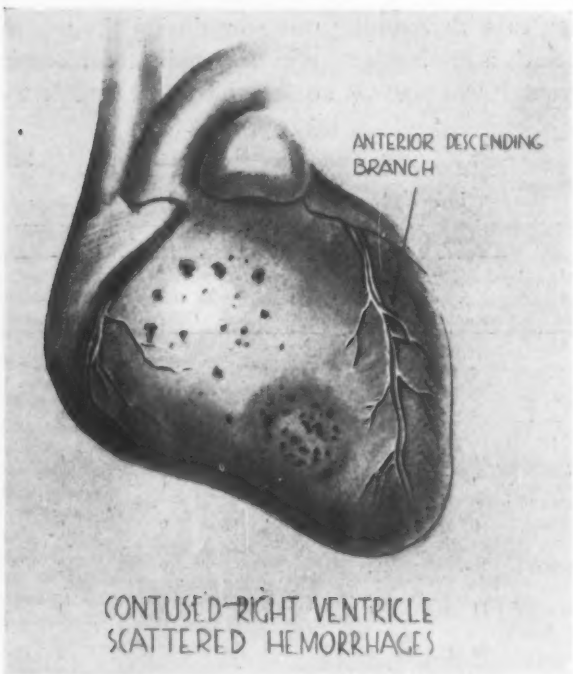

FIG. 1.—This patient was wounded by high velocity machine gun bullets and he suffered a long gutter-wound of the sternum with multiple fractures of the cartilages on the left. There were scattered patchy contusions of the right ventricle with an area of confluent intramuscular hemorrhage and softening near the apex. "Cardiac" death 35 hours after wounding.

PATHOLOGY

The cardiac lesions which were seen at surgery or autopsy have been classified as follows: Myocardial contusion; pure lacerated or incised-type wounds; laceration with myocardial contusion; penetrating and perforating wounds of the chambers; embolus to the heart (see Tables II and III). Cases in which foreign bodies were found in the myocardium or chambers were placed in the various pathologic categories depending upon the type of myocardial injury produced, irrespective of whether or not the foreign body was

still present. In general, the signs and symptoms exhibited, the indications for surgery, and the causes of death, differed in the various pathologic categories.

Insofar as operative therapy is concerned, contusive lesions of the myocardium are non-surgical. Pathologically they are apparently identical to the contusions resulting from blunt trauma to the chest and from "steering wheel" injuries which have been described by Beck[2] and Elkin.[3] In most battle-incurred contusions, however, the pathogenesis is different in that the contusive force often is propagated by the passage of missiles of varying size and usually high velocity in the immediate vicinity of the heart. The wounding

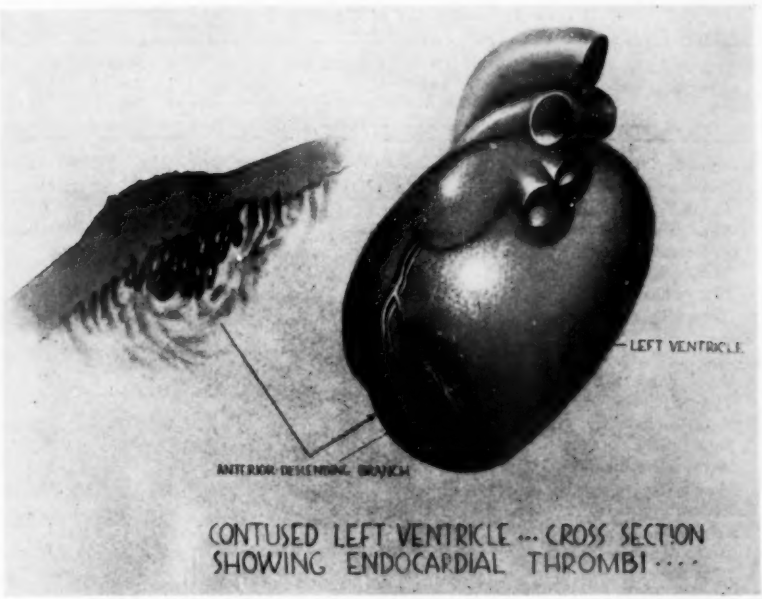

FIG. 2.—This patient sustained an extensive tangenial sucking wound of the left chest antero-laterally. Rib fragments, apparently acting as secondary missiles, caused a severe localized contusion of the left ventricle with superficial laceration of the epicardium and thrombosis of the epicardial veins. The pericardium was intact. Hemorrhage extended through the myocardium to the endocardium. Mural thrombi were present in the chamber of the ventricle. "Cardiac" death on the operating table, 17 hours after wounding.

power of a missile is believed to be more directly proportional to its velocity than to its size or shape.[4] Thus, a high rate of energy is imparted to the tissues in the track of the missiles and particles of tissue thrown laterally pass their energy on, producing further damage. In at least two patients, extensive myocardial contusion resulted from fractured ribs or sternum acting as secondary missiles. Among the pericardial cases, two wounds were caused directly by rib fragments. Such a sequence was found particularly in tangential wounds. None of the contusions in this series was believed due to "blast," *i.e.*, a positive pressure wave in the atmosphere.

In contusive lesions, the pathology consists of scattered or confluent petechial hemorrhages involving the myocardium over varying areas of one or two chambers (Fig. 1). The hemorrhage may extend through to the endocardium. With actual injury to the endocardium, or with subendocardial hemorrhage, adherent mural thrombi may develop. These have been found in five cases at autopsy (Fig. 2). When extensive lesions are scattered along the acute or obtuse margin of the heart, the hemorrhage may involve the myocardium of both ventricles and extend into the interventricular septum. Superficial abrasions of the epicardium and engorgement or thrombosis of the sub-epicardial

TABLE III.—*Deaths in Cardiac Lesions.*

Lesion	Ventricle			Auricle		Right Auricle Right Ventricle	Total
	Left	Right	Both	Left	Right		
Contusion							
Total deaths	4	4	2	0	1	0	11
Death due to heart	3	2	1	0	0	0	6
Type of cardiac death	(c, c, x)	(c, x)	(x)				(6)
Pure laceration							
Total deaths	7	2			1		10
Due to heart	1						1
Type of cardiac death	(c)						(1)
Laceration and contusion							
Total deaths	2	1	2				5
Death due to heart	1	1	2				4
Type of cardiac death	(c)	(c)	(c, c)				(4)
Perforated chamber							
Total deaths	2	1		1	5		9
Death due to heart	2	1		1	4		8
Type of cardiac death	(c, h)	(t)		(c)	(h, h, h, t)		(8)
Embolism to heart							
Total deaths		1					1
Death due to heart		1					1
Type of cardiac death		(c)					(1)

In Tables III, VI, VII, and VIII, all figures in parentheses represent deaths due to the heart itself. Each *symbol* within the parentheses represents a single case of death due to the heart:

(c)=Death due directly to the cardiac lesion. Usually sudden or rapid death from infarction, fatal arrhythmias, or lethal myocardial damage.....11 cases
(h)=Death due to exsanguination from the heart..... 4 cases
(t)=Death due directly to tamponade..... 2 cases
(x)=The heart lesion an essential contributory cause of death..... 3 cases

vessels are often found. When a major artery is contused sufficiently, thrombosis is probable. The myocardium may show gross evidence of degeneration or actual necrosis. Microscopically, there is interstitial hemorrhage which varies in severity and extent. The muscle fibers show fragmentation, loss of striation, or advanced necrosis. Eosinophilia, leucocytic infiltration, and beginning phagocytic removal of necrotic muscle have been observed as early as 18 hours following injury.

In the group of contusions there was a death rate of 37.5 per cent due to the cardiac lesion itself (Table III). Of the 16 cases of myocardial contusion, nine had an intact pericardium.

The other types of myocardial damage listed above may be classified as "potentially surgical" lesions. In the laceration category are placed all cases with incised-type or cleanly lacerated wounds of the myocardium in which there was no gross evidence of myocardial contusion or necrosis. Two cases with foreign bodies in the myocardium are included here since the myocardial wound fitted this classification pathologically. The less serious nature of this type of wound is demonstrated by the single death due to the heart in ten cases of pure lacerated wounds.

When lacerated wounds are associated with extensive contusion, the lesion is a serious one. In this group the typical gross appearance is that of a myocardial laceration, the edges of which are elevated and discolored and show areas of hemorrhage. The edges may be friable so that attempted suture and approximation are fraught with difficulty. In this category there was a 40 per cent death rate due to the heart.

In wounds penetrating to the chambers of the heart, hemorrhage is the most frequent complication and the most important cause of death. The hemorrhage may be slight, exsanguinating, or cause tamponade. Frequently, penetrating or perforating wounds of the chambers do not result in exsanguination because the missile may pass through the myocardium at an angle so that the wound is partially closed. A small penetrating wound may become occluded by clot. The position of the right auricle offers some protection in wounds of this chamber since the lung may collapse against the auricle and temporarily control hemorrhage. As with other cardiac wounds there may be associated laceration and contusion of the myocardium which complicate surgery and repair. The death rate due to the heart among cases of wounds penetrating the chambers was 42 per cent.

There were six cases of perforating (through and through) wounds of the chambers in this series. Two occurred in the left ventricle and both survived following suture. One of these cases has been reported in detail elsewhere.[5] In four cases of perforation of the auricles there were three deaths. No case of perforation of the interauricular or interventricular septum survived to reach a forward hospital.

Instances of foreign body embolism to and from the heart form a small but interesting group. There were four examples in this series. In two the missile came to rest in the right ventricle by way of the inferior vena cava. In one of these the situation was recognized and a 45 caliber bullet successfully removed.[5]

In the other case the shell fragment "disappeared" after having entered the body through the right flank. The initial thoracic roentgenogram revealed the questionable presence of a missile just above the left diaphragm near the midline. The films were repeated later using soft tissue penetration technique and the foreign body was not visualized. Over a period of nine days the patient had attacks characterized by decreased blood pressure, high fever, mental confusion, pallor, rapid pulse, and "shocky" appearance. Malaria was suspected and the patient appeared to improve temporarily on quinine ther-

apy. In retrospect the attacks could well have been due to myocardial ischemia. Sudden death occurred ten days after wounding. At autopsy the right ventricle was found to be greatly dilated and the myocardium overlying the foreign body was hemorrhagic and necrotic (Fig. 3). Early removal of the shell fragment from the chamber of the right ventricle probably would have been life-saving.

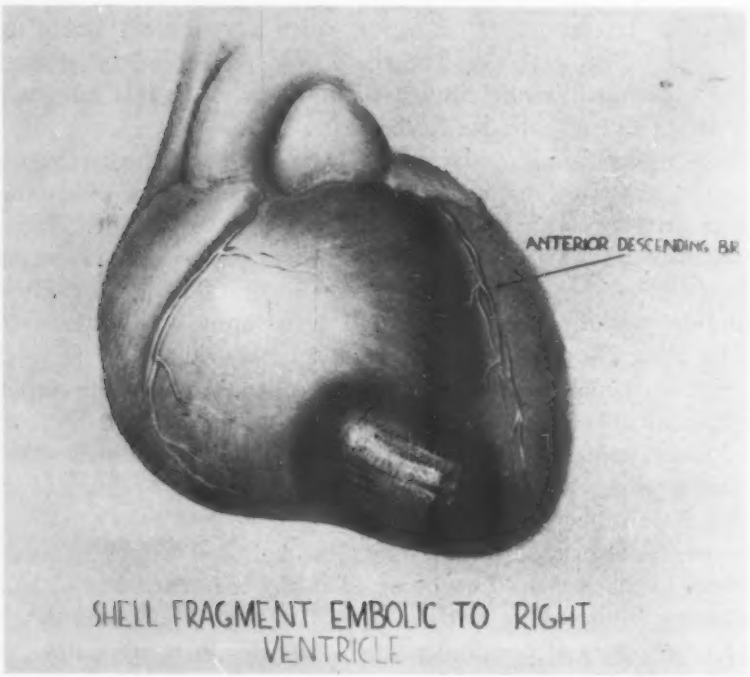

FIG. 3.—Semi-schematic transparency of a shell fragment, 20x15x10 mm. which became embolic to the right ventricle by way of the inferior vena cava. The overlying musculature was hemorrhagic and necrotic over an area 4 x 5 cm. near the apex. The right ventricle was greatly dilated. Sudden death 10 days after wounding.

As an embolus from the heart, the foreign body may enter the pulmonary circulation, become retrograde in the systemic venous circulation, or enter the systemic arterial vessels. In one case in this series the missile entered the right auricle, dropped into the inferior vena cava, and eventually was recovered from the left common iliac vein.[6] In the fourth case a bullet entered the left ventricle and came to rest in the right flank region, presumably in the right common iliac artery. The patient had no symptoms of arterial obstruction.

OPERATIVE TREATMENT

Ten of 16 lacerated wounds of the myocardium which were exposed at operation were not repaired (Table IV). There seemed to be no immediate ill effect resulting from lack of repair. Further, of the cases of laceration seen at autopsy only, none of the deaths were believed to be due to lack of repair. A repair was listed as complete if the edges of the laceration had been entirely approximated with sutures (Fig. 4). Partial repair (two cases) was that in which complete approximation of the edges could not be obtained and pericardium was used to help bridge the defect (Fig. 5). The pericardium was frequently employed as a secondary covering being either sutured over

TABLE IV.—*Incidence Repair Heart Lesions.**

		Ventricle			Auricle		Right Auricle Right Ventricle	Total
		Left	Right	Both	Left	Right		
10 Lesions seen autopsy only	Lac.	1	1	2	0	0		4
	Perf.	1	1		1	3		6
29 Lesions seen at operation	Lac.	11	3	0	0	1	1	16
	Perf.	6	2	0	1	4	0	13
		19	7	2	2	8	1	39
Of 29 cases visualized at operation:								
Complete repair of	Lac.	1	2	0	0	0	1	4
	Perf.	6	1	0	1	2	0	10
Partial repair of	Lac.	2	0	0	0	0	0	2
	Perf.	0	0	0	0	0	0	0
No repair	Lac.	8	1	0	0	1	0	10
	Perf.	0	1	0	0	0	0	1
Repair attempted and failed	Lac.	0	0	0	0	0	0	0
	Perf.	0	0	0	0	2	0	2

Laceration=Wounds with and without contusion.
Perforation=Penetration or perforation of chambers.
* 39 lesions exclusive of pure contusions and embolus to the heart.

the closed wound or sutured to the lips of a poorly approximated wound. The edges of the pericardium were imbricated in some cases to give additional strength. When the pericardium was sutured over a myocardial wound it was first drained posteriorly. Note was made in two cases of the use of free muscle grafts to aid in the control of bleeding.

Of 13 wounds involving the cardiac chambers, complete closure was obtained successfully in ten. One wound was not bleeding at the time of operation and was not sutured. In two auricular wounds, closure could not be accomplished and the patients died of uncontrollable hemorrhage. In both, attempts were made to plug the defect in the auricular wall with the finger.

The foreign body was described as in the heart or pericardium in 21 cases. The typical removal of a foreign body is shown in Figure 6.

These figures show a low percentage of removal. The majority not removed were small fragments, 0.5 cm. or less. In several, the condition of the patient did not warrant further search. The foreign bodies marked "probable" were not definitely located but from roentgen evidence and operative findings, their presence in the pericardial sac seemed likely. Of the eight foreign bodies found at autopsy, the missile was directly responsible for one death (embolus to the heart) and possibly for a second death. (See also Analysis of Deaths.)

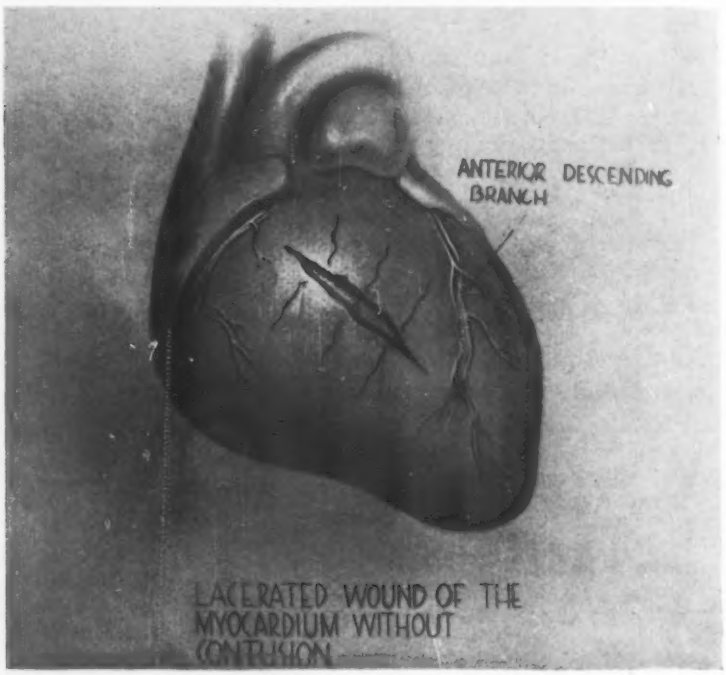

FIG. 4.—Incised-type lacerated wound of the right ventricle without gross myocardial contusion. In repair the sutures were passed through the muscle just at the bottom of the laceration and not through the endocardium. Recovery.

THE PERICARDIUM

There were 18 cases in which the pericardium alone was injured. In 14 the wounds were lacerated and in four, foreign bodies were embedded in the pericardium. Two of these were metallic and two were rib fragments. Of all the wounds in which the pericardium was opened it was sutured tightly in five cases; in the remainder the pericardium was drained into the pleural cavity. In two of the five cases (one, a pure pericardial injury and one a myocardial wound) there was massive troublesome pericardial effusion postoperatively. This was not noted in any of the cases which were drained.

POSTOPERATIVE FINDINGS

In the patients that lived, certain findings relative to the heart were recorded. Eight patients developed friction rubs approximately 24 hours postoperatively and some of these were audible up to three weeks. One patient had numerous extra systoles for three days following operation. Three patients suffered significant myocardial accidents during the postoperative period. One showed mild symptoms and signs of myocardial infarction 19 days following a self-inflicted stab wound. The second patient had had extra systoles preoperatively. He developed sudden precordial pain, circulatory collapse and transient auricular fibrillation 24 hours after operation (33 hours after injury). Frequent extra systoles were present for 14 days thereafter. At operation there was a clean superficial laceration of the left ventricle at the apex and it was necessary to ligate a terminal radicle of the anterior descending branch which was continuing to bleed. The third patient had a repair of a wound which penetrated to the left ventricular chamber. Fifteen days following operation he was suddenly seized with severe precordial pain. Dyspnea, cyanosis, and pulmonary edema developed. Acute left ventricular failure was diagnosed. He was somewhat improved in four hours and was asymptomatic by the end of 48 hours.

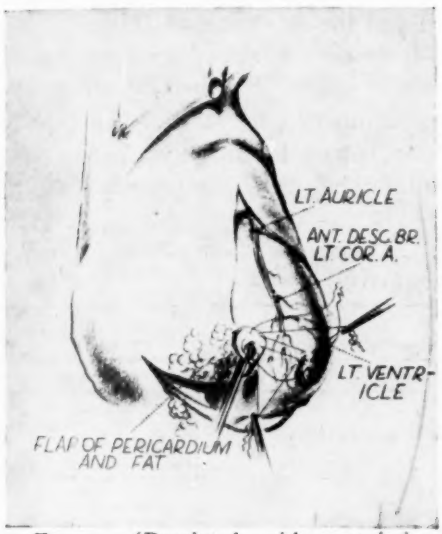

FIG. 5.—(Reprinted with permission from Surgery, **20**: 373, 1946). Use of pedicled graft of pericardium in strengthening the repair of a lacerated perforating wound of the left ventricular chamber. In this case the muscle sutures did not entirely arrest bleeding. Recovery.[5]

One patient developed complete right-sided hemiplegia. At operation, a 3 cm. laceration of the left ventricle was discovered. A second patient with a lacerated wound of the left ventricle entered the shock ward with a cold, pulseless left foot which did not completely return to normal for 36 hours. One must consider the possibility that the complications in these two cases were due to emboli resulting from the detachment of mural thrombi in the left ventricle.

ANALYSIS OF DEATHS

There were 30 deaths in the entire series. Three were among the 18 cases of pericardial wounds. All of these occurred more than 48 hours following operation and none was due to the pericardial involvement. Twenty-seven deaths occurred among 57 patients with myocardial lesions; of these, 20 were

due directly to the heart. This is a "cardiac" death rate of 35 per cent. The remaining seven deaths were due to the severity of thoracico-abdominal or esophageal wounds, shock, bronchopneumonia, and anuria.

Tables VI and VII give a breakdown according to time and cause of death. Of the 11 "myocardial" deaths (c), four were in poor condition on admission and died either before or during operation. One was apparently in good condition and died suddenly during operation. Six died postoperatively. Three of these died suddenly and without warning; three died shortly after symptoms of myocardial infarction had developed. In the three cases where the heart was considered an essential contributory cause of death (x), the cardiac lesion was extensive in all. Other wounds were also severe and it cannot be said, therefore, that the heart was the sole cause of death.

In Table VIII the cardiac deaths have been analyzed with reference to the possible surgical correction of the cardiac lesion. This includes the removal of foreign bodies and the suture of lacerations or perforations. As expected, none of the contusions could have been helped by surgery. In the single patient with pure myocardial laceration who died immediately following

TABLE V.—*Fate of Foreign Bodies*

	Pericardium	Pericardial Sac	Myocardium	Completely in Chamber
Number of cases	4	3 (2 probable)	10	4 (2 embolic)
Removed at operation	4	1	3	1 (embolic)
Not removed	0	2 (both probable)	7	3
Found at autopsy			(5)	(3)

surgery, there is no evidence that suture would have been beneficial. In this case there was an early pericarditis from contamination by stomach contents, but its significance cannot be evaluated. Of five cases of myocardial laceration and contusion (including one repaired perforation), the damage appeared to have been lethal in four and no conceivable further repair would have changed the fatal outcome. In three of these, for example, the anterior descending branch of the left coronary artery had suffered a traumatic thrombosis for at least half its length while the fourth patient again had an early pericarditis from contamination with stomach contents. The fifth case, in the "possibly benefited" column, concerns a retained foreign body. In this instance the patient died suddenly four hours following débridement of his thoracic wound. At autopsy a shell fragment, 15x10x10 mm., was found lying in contact with the sternum. It was in a shallow, contused, lacerated wound of the right ventricle at the base of the pulmonary conus. It is possible that the continued presence of the foreign body was instrumental in propagating fatal ectopic stimuli. Removal might well have been beneficial. The pericardium contained 150 cc. of liquid blood, but it was not tense, and the mode of death did not seem to be that of pressure from tamponade.

The fatal embolus to the right ventricle has been described previously. Its early removal probably would have been life-saving.

As might be expected, the largest group which could have benefited from surgery was that in which penetration of the chamber had occurred. Successful repair of the defect in the six cases listed would probably have been life-saving. Of the four dying from exsanguination (h), one died in the shock ward and two died on the table. The fourth case had an unrecognized perforating wound of the right auricle. The patient's original hemorrhage seemed to have ceased at the time of débridement of the thoracic wall, but there was rapid exsanguination before further surgery could be performed 36 hours after

TABLE VI.—*Total Deaths* (Among 57 cases with myocardial wounds)

Time of Death	Pure Thoracic	Thoraco abdominal	Total
Preoperative			
Total deaths	1	1	2
Due to heart	(h)	(c)	(2)
During or immed. postoperative			
Total deaths	5	5	10
Due to heart	(c, c, h, t)	(c, c, h, t)	(8)
1–5 hours postop.			
Total deaths	1	3	4
Due to heart	(c)	(c, x)	(3)
6–12 hours postop.			
Total deaths	0	2	2
Due to heart	(0)	(0)	(0)
13–24 hours postop.			
Total deaths	5	1	6
Due to heart	(c, h, x)	(c)	(4)
25–48 hours postop.			
Total deaths	0	1	1
Due to heart	(0)	(x)	(1)
Over 48 hours postop.			
Total deaths	1	1	2
Due to heart	(c)	(c)	2
Deaths (total)	13	14	27
Due to heart	10	10	20

injury. One of the two fatal cases of tamponade (t), was entirely unsuspected. The second case was recognized too late, although it is probable that the patient eventually would have died from his severe thoracico-abdominal wounds. The mode of death in the seventh case (c), is difficult to explain. Death was sudden and, therefore, probably due to myocardial dysfunction. The patient had a through and through wound of the left auricle. There was approximately 100 cc. of blood in the pericardium although no evidence of tamponade. One can only speculate as to whether or not repair of the defects would have been successful in preventing the immediate death. It is probable, however, that the patient could not have long survived without repair.

THE TIME AND PLACE FOR CARDIAC SURGERY IN WAR WOUNDS

It is particularly difficult to decide these matters when confronted with war wounds of the heart. When a cardiac wound is suspected, a judgment should be made if possible as to the type of pathology present and as to the presence or absence of a foreign body in the heart or pericardium. Three questions must be answered: (1) Can the cardiac lesion itself be corrected by surgery? (2) If so, should this surgery be performed in a forward hospital or at the base? (3) What is the effect of the cardiac status on the patient's ability to withstand needed surgery for other wounds? By contrast to civilian cardiac wounds, the heart in war casualties is often but one of several organs involved and both the diagnosis and the decision as to time of operation are compliated by the presence of multple injuries.

The problem may be partially simplified by considering each type of myocardial injury more or less separately. When a contusion is suspected, decision must be made as to when to operate on concomitant wounds. As

TABLE VII.—*Time of Occurrence of Deaths Due to Heart, Segregated by "Lesion."*

Cardiac Lesion		Number of deaths occurring: Preop.	During or Immed. p. o.	1–5 hr. p. o.	6–12 hr. p. o.	13–24 hr. p. o.	25–48 hr. p. o.	Over 48 hr.
Contusion	(6)	(c)	(c)	(x)		(c, x)	(x)	
Pure lac.	(1)		(c)					
Lac. and contus.	(4)		(c)	(c, c)		(c)		
Perf. chamber	(8)	(h)	(c, h, h, t, t)			(h)		(t)
Embolus to ht.	(1)							(c)
Totals	(20)	(2)	(8)	(3)		(4)	(1)	(2)

stated above, the contusion, *per se,* is not a "surgical" lesion. The fact that six of 11 deaths in the contusion group were due to the heart shows that these patients were not good operative risks. The diagnosis of a cardiac contusion should not be extremely difficult since it has been noted in the present series that the majority of signs and symptoms indicative of anoxia and of cardiac dysfunction (persistent dyspnea, tachycardia, arrhythmia, etc.) were found in patients who had significant contusions of the myocardium.

In myocardial contusion, the clinical and pathologic picture is thus similar to that in myocardial infarction following coronary thrombosis, and we have felt that these patients might well be handled as if they had an acute coronary occlusion. If this analogy be carried further, then the first 24 to 48 hours is an extremely critical time for surgical intervention since the danger of cardiac standstill and lethal arrhythmias may be enhanced by anesthesia or operative manipulations. In many cases, however, attention must be given to other serious concomitant trauma, especially thoracic-abdominal wounds where undue delay in surgery usually is disastrous. Under these circumstances it is

best to prepare the patient as thoroughly as possible consistent with the major *surgical* lesion. The mortality rate in such cases inevitably will be high. There remains a group of cases with purely thoracic wounds in which early surgery (within six to 12 hours) is not mandatory and wounds in which delay, because of a cardiac contusion, may be practicable.

Viewed from this standpoint the cases of contusion were reviewed. There were three, all with a fatal outcome, in which it was felt that further delay in surgery probably would have been beneficial. Two had thoracic wounds and one had a high thoracico-abdominal wound in which it was obvious that only the liver was involved. The time lag between wounding and surgery was 17, 11, and 5 hours respectively. In each instance, signs of cardiac dysfunction were prominent. During resuscitation the patients remained in poor general condition in spite of an increase of the blood pressure to 95 or above. Rapid pulse, dyspnea, and semi-stupor were out of proportion to the obvious intrathoracic damage. In each instance death occurred during, or shortly following

TABLE VIII.—*Cardiac Fatalities (20) With Reference to Surgical Correction.*

Cardiac Lesion No. of Deaths		Would Have Been Benefited by Surgery	Possibly Would Have Been Benefited	Could Not Have Benefited From Surgery
Contusion	6	0		6
Pure lac.	1	0		1
Lac. and cont.	5*	0	1 (c)	4
Perf. chamber	7	6 (h, h, h, h, t, t)	1 (c)	
Embolus to heart	1	1 (c)		
	(20)	(7)	(2)	(11)

* This includes one case of perforation of chamber which was successfully repaired but died a "myocardial death" because of extensive laceration and contusion.

surgery. We have also studied the record of a fourth case (not included in this series) in which there was a single thoracic wound, a six hour lag, and sudden death on the operating table. At autopsy this patient showed extensive contusion of the right ventricle and thrombosis of the anterior descending branch of the left coronary artery. While any of these four patients might well have died without operation, surgery could not be deemed mandatory at the time it was performed. The added burden of an anesthetic and an operative procedure cannot be ignored as probably precipitating the fatal outcome.

In contrast to the relatively early surgery in these four patients, two other cases may be cited in which initial surgery was considerably delayed (three and five days after wounding). Both were in shock on admission to the hospital and cardiac contusions were diagnosed. In one, a friction rub was audible 24 hours after wounding and the pulse remained over 120 beats per minute for 48 hours. The second patient had intermittent periods of cardiac arrhythmia for four days, associated with excessive bronchial secretions and jaundice. Both patients recovered from surgery. It was our strong feeling that operation

performed in either case at 12 hours or less might have ended disastrously. In summary, when a cardiac contusion has been diagnosed and indications for early operation such as continuing hemorrhage or thoracico-abdominal involvement are not present, surgery probably should be postponed for a minimum of 48 hours, to give every opportunity for myocardial irritability to regress.

The feasibility of early thoracotomy for the express purpose of suturing cardiac lacerations cannot be settled. With cleanly-lacerated or incised wounds there are few if any symptoms of cardiac dysfunction and damage to the heart can only be suspected from the course or location of the missile or from a possible tamponade. Of the lacerations exposed surgically in this series of cases only 38 per cent were repaired and there appeared to be no immediate disability from lack of repair. Certainly some lacerations should be untouched since attempts at suture may lead to further difficulties. Such wounds include the superficial, non-bleeding lacerations of one or two mm. in depth, particularly if they involve the musculature of the left ventricle; round or oval lacerations especially in the region of the apex; and lacerations near a major coronary vessel, the repair of which might cause thrombosis. Shallow ovoid lacerations frequently remain after a superficial foreign body is removed (Fig. 6) and repair may not be necessary. When the heart is exposed for any reason, however, the suture of certain lacerations is better accomplished at a forward hospital. It is probable that no efficient repair can be performed in a base section hospital ten or more days after injury. Retraction of edges of the myocardial defect and induration from fibroblastic tissue proliferation combine to defeat a good approximation.

Penetrations or perforations of the cardiac chambers are usually manifest by continuing hemorrhage and early surgery is mandatory. If foreign bodies are found or if it is suspected that they are in the chambers, an attempt should be made to remove them at the same time, but it should be remembered that the main indication for operation at this time is the control of hemorrhage. Long-continued search or blind manipulations within the chambers are not justified. If the missile is not found almost immediately, the defect should be sutured and further consideration given to removal of the intracardiac fragment at a base hospital.

If the bleeding causes tamponade rather than exsanguinating hemorrhage, the treatment may be more individualized. Should the tamponade develop rapidly it is probably better to operate at once, particularly if it is known that the missile causing the injury is large. If, however, the tamponade develops slowly, one or two aspirations may suffice as has been suggested by Strieder[7] and Blalock,[8] and major surgery may not be necessary.

When foreign bodies are suspected of being in the pericardium or myocardium their removal should be postponed until the patient can be evacuated to a base section center unless hemorrhage persists or symptoms of cardiac dysfunction recur. Two other factors enter into the considered opinion for recommending a delay in the removal of cardiac foreign bodies. In the present series, nine of the 13 missiles believed to be in the pericardial sac or myo-

cardium were not removed. Furthermore, Harken[9] in a base section thoracic center operated on 56 patients for the removal of missiles from the heart or pericardium. None of these patients died.

Metallic foreign bodies may come to rest in a cardiac chamber either by traversing the myocardium directly or by embolism through the pulmonary or systemic venous system. Cases of foreign body embolism to the heart are now

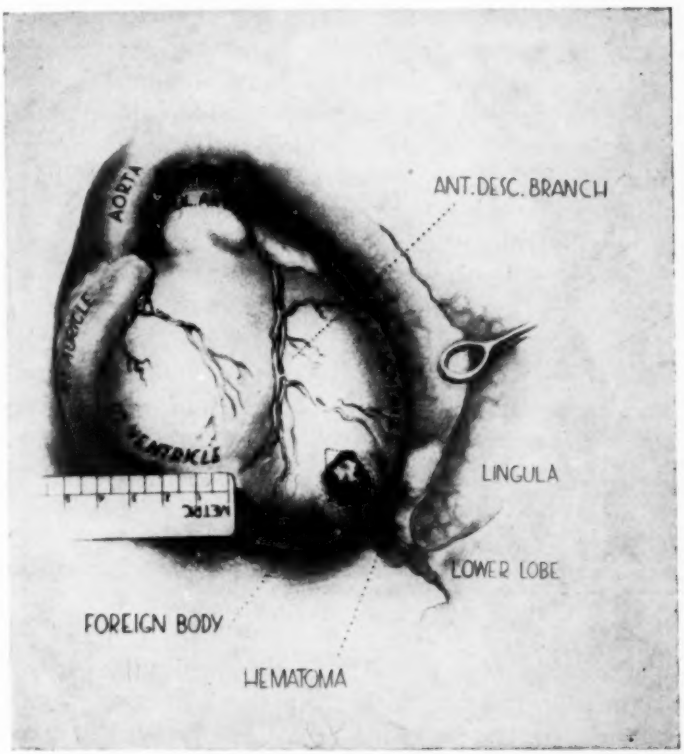

FIG. 6.—(Reprinted with permission from J. Thor. Surg., 15: 1, 1946.) A case in which the shell fragment was removed 40 hours after injury. Cloth was attached to the foreign body. The missile was known to be in the myocardium and was relatively large (20 x 13 x 9 mm). The myocardial defect was oval and the muscle at the edges was necrotic and soft. No repair of the muscle was attempted but the pericardium was sutured over the defect. Recovery. (Illustration courtesy of L. A. Brewer.[20])

being recognized more frequently. In the past, their removal has been the subject of much discussion.[1, 10, 11] While some intracavitary missiles have remained asymptomatic, others have caused death from primary pulmonary embolism;[12, 13] secondary pulmonary embolism;[14] focal infection;[15] and direct myocardial damage.[16] In one of Harken's[17] cardiotomies myocardial thinning was seen in the right ventricle overlying an embolic shell fragment.

In 1938 Decker reviewed 20 personal and collected cases of foreign bodies which were free in the cardiac cavities. Four of these were subjected to cardiotomy with one death (25 per cent); 16 were not operated upon and there were nine deaths (56 per cent). It is apparent that improved surgical technic and better anesthesia have combined to reduce greatly the risk of cardiotomy. Witness Harken's recent series of 13 cases in which intracavitary missiles were removed with no mortality.

Our present attitude regarding "potentially surgical" war wounds of the heart may be summarized as follows: The only absolute indication for early cardiac surgery in forward hospitals is continuing severe hemorrhage or immediate cardiac tamponade. When the heart is normal in size and there are no disturbances of physiology, mere suspicion of a cardiac wound is not, in itself, sufficient indication for early thoracotomy. All patients who remain asymptomatic during the early period after wounding should be evacuated without specific cardiac surgery for final study and evaluation in a specialty hospital. If the patient is admitted to a forward hospital with signs of cardiac dysfunction (disproportionate dyspnea, arrythmias, etc.) it is probable that myocardial contusion is present. This finding demands that all surgery be postponed for at least 48 hours whenever possible. When *delayed* or recurring episodes of myocardial irritation, bleeding or infection occur, corrective surgery should be undertaken in forward hospitals for the removal of foreign bodies and the repair of lacerations.

Nearly all intracavitary missiles should be subjected to delayed removal at a base section center. On the other hand, recognition that the foreign body in the chamber is causing cardiac disability or is the source of secondary emboli, constitutes an indication for early removal in a forward hospital.

COMMENT ON EXPOSURE AND SURGICAL TECHNICS

When a "surgical" cardiac wound is diagnosed, adequate exposure through an elective approach is mandatory. In the presence of exsanguinating hemorrhage, for example, the tragedy of inadequate exposure has been experienced. For most purposes an anterior approach is greatly preferable and an intercostal incision always should be employed unless the corresponding rib is badly fractured. The third or fourth intercostal space offers the best exposure for the auricles and the fifth or sixth for the ventricles. In general, more of the right ventricle can be exposed through a *left-sided* incision than through a right-sided thoracotomy.

The incision should be carried to the sternum and the internal mammary vessels ligated and divided. When necessary, increase in vertical exposure may be obtained by division of one or more cartilages. Further horizontal exposure is facilitated by transverse section of the sternum at the level of the intercostal incision.[9] The approach should be transpleural in all instances. We believe strongly that no time should be wasted in attempting an extrapleural operation. Such a procedure takes longer, exploration is more difficult and the exposure is not as satisfactory particularly for posterior wounds. In

addition, the usual hemothorax makes extrapleural exposures impractical. While it has not been employed by us, mention should be made of median extrapleural sternotomy of the Duval Barasty type,[1] for cardiotomy on the right heart. Both auricles and ventricles are exposed simultaneously and the possibilities of missile migration from one chamber to another may thereby be lessened.

Ten cc. of 5 per cent procaine usually have been injected into the pericardial sac for several minutes before exposing the heart. This materially cuts down the incidence of ectopic beats while the heart is being handled. Several

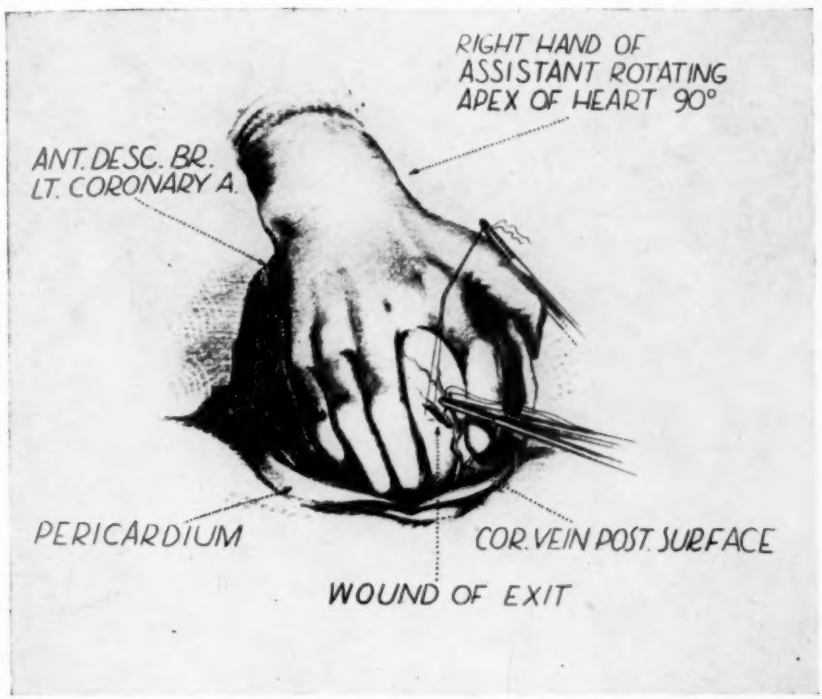

FIG. 7.—(Reprinted with permission from Surgery, **20**: 373, 1946.) Forward rotation of the apex of the heart by the hand of the assistant surgeon. The diaphragmatic surface of the heart can thus be well visualized. By spreading the fingers any portion of this surface can be readily sutured.[5]

maneuvers have been employed in manipulating the heart. For anterior lesions, the "palming" method,[1] or the Sauerbruch grip has advantages. By the former means the third, fourth and fifth fingers are passed behind the heart, the index finger is passed in front, and the thumb is free to apply hemostasis or lateral pressure in stabilizing a missile. In exposing the diaphragmatic surface, some surgeons prefer the apical suture. The writer, however, has felt that the hand of the assistant makes a much better retractor (Fig. 7). The apex of the heart can thus be rotated nearly 90° forward and the cardiac movements are con-

siderably dampened. By spreading the fingers a slotted type of retractor can be simulated which will expose any portion of the wall.[5]

We owe much of our knowledge of suturing technics to the well-known writings of Beck, Elkin, Bigger,[18] and others. The general principles which they have promulgated form the background for most cardiac repair. Our chief concern here is in the emphasis on certain technics which are particularly valuable in dealing with large wounds. Suture material should be of braided oo or ooo silk, preferably oiled or waxed. A small-eyed or atraumatic

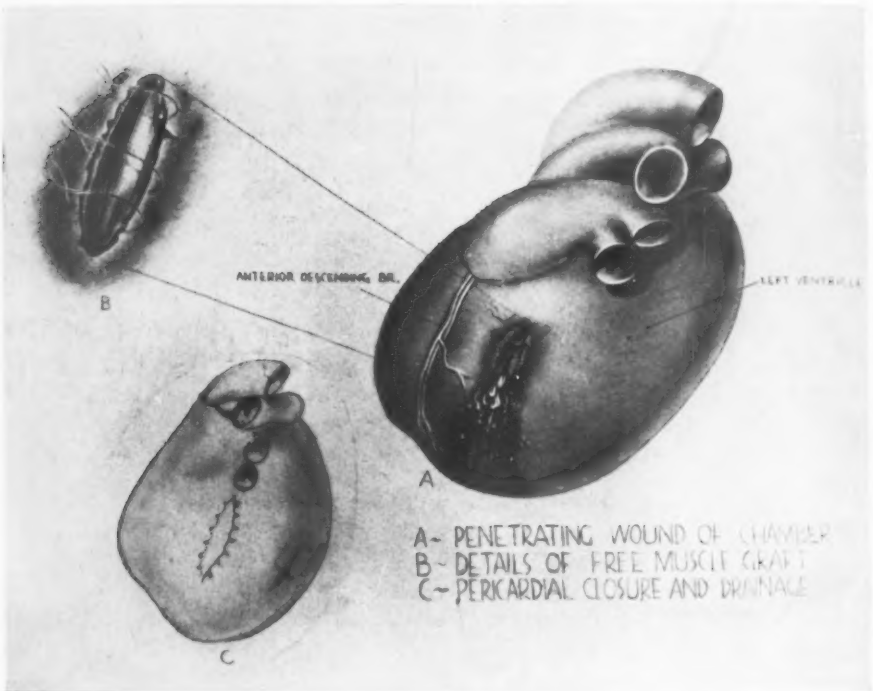

FIG. 8.—Ideal repair of a penetrating wound of the ventricular chamber with laceration, contusion, and softening of the muscle. The repair makes use of a free graft of voluntary muscle and imbrication of the pericardial edges over the myocardial defect. Note the posterior drainage of the pericardium.

needle should be used. Interrupted sutures always should be employed and should be placed close to the edge of the wound. They should be tied without undue tension, and during systole if possible. Pressure necrosis of the wound edges, particularly in wounds involving the chambers may lead to secondary fatal hemorrhage. The sutures should not be passed through the endocardium as this increases the possibility of thrombus formation (Fig. 4). In the repair of auricular wounds, however, this may be impossible to avoid. In general, lacerations of the right ventricle are easier to repair than those of the left

and since the wall of the right ventricle is thinner, it should be repaired more often. The justification for repair lies in the fact that the scar from a repaired laceration is stronger and the wall is thicker than if no repair is performed. Complete suture, or repair of some type is necessary if the bottom of the laceration feels thin or if there is any bulging. Without adequate suture in cases of this kind, later aneurysm of the myocardium may result and instances have been reported by Loison.[19]

Some lacerations because of loss of substance, or surrounding contusion and necrosis are difficult if not impossible to suture completely. Considerable

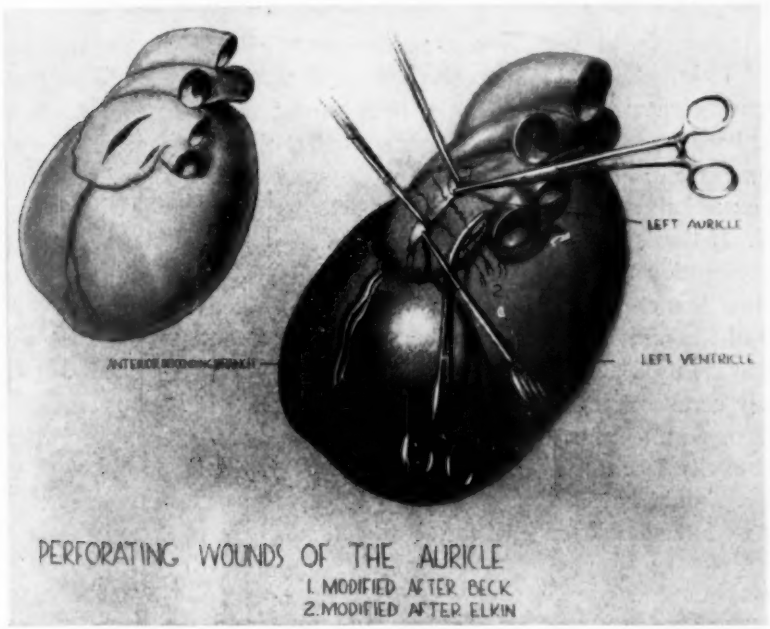

FIG. 9.—The closure of large auricular wounds: 1. Modified after Beck (see text); 2. Modified after Elkin (see text).

ingenuity must be exercised, particularly if a chamber has been opened. Free muscle grafts are useful in this connection and should be employed more frequently. They can be laid in the defect and held in place by fine sutures. This not only helps to fill the defect but is instrumental in stopping hemorrhage or myocardial ooze (Fig. 8). As a further reinforcing mechanism, the pericardium always should be sutured over the area of repair (after first providing drainage more posteriorly into the pleural cavity through a cruciate incision). The edges of the pericardium may be used and, when necessary, sutures may be taken into the epicardium or myocardium at the edge of the defect (Fig. 5). The pericardium combines very nicely with a free muscle graft in giving a solid repair.

Wounds penetrating the chambers of the heart should be sutured even though not bleeding when first exposed. Later loosening of clot may lead to secondary hemorrhage if the wound has not been repaired. Large wounds of the auricles deserve special mention. Even a 3 cm. wound of the auricle may not lead to immediate exsanguination. The lung may collapse against the auricle or a clot may form, each preventing fatal hemorrhage. The usual maneuver of occluding the defect with a finger, as employed in penetrating wounds of the ventricles, cannot be used in auricular wounds because of the thinness of the wall. If sutures cannot be placed at once, each edge of the auricular wall should be grasped with one or two fine hemostats. These may then be held in approximation or ligated temporarily until sutures can be properly placed (Fig. 9). If the wound is at the edge of the auricle it can be completely occluded with a rubbershod forceps while the wound is being sutured (Fig. 9). Perforating (through and through) wounds of the chambers may be repaired successfully if both wounds can be exposed. No means has yet been discovered of repairing a wound of the posteromesial (or mediastinal) surface of the right auricle. Two patients with this type of wound died from exsanguination but in both the hemorrhage came from the "free" wound. If the latter could have been repaired it is possible that the mediastinal perforation would have sealed off.

When branches of the coronary arteries are bleeding careful ligature or suture of the individual branch is necessary. If fine metal clips are available they may be used as Beck has suggested.

Only certain aspects of closure need comment. We have used interrupted silk throughout. The pericardium should be drained posteriorly into the pleural cavity by means of a cruciate incision. If the sternum has been transected it should be wired firmly. In the presence of extensive intrathoracic injury we have employed intercostal water seal drainage of the pleural cavity.

SUMMARY

1. Seventy-five cases of war wounds of the heart and pericardium were given initial care by surgeons of the Second Auxiliary Surgical Group. This series comprised three and three-tenths per cent of all intrathoracic wounds operated on by members of the unit.

2. The cases have been reviewed with regard to diagnosis, pathology, operative treatment and postoperative course.

3. The causes of death have been analyzed with respect to the cardiac lesion and the probable influence of surgical intervention.

4. Based on observations of the participating surgeons and from personal experience both in forward and rear echelon hospitals, deductions have been made as to the advisability of early or delayed surgery in certain types of cases.

5. Comment has been made on operative approach and technic, emphasizing particularly the problems encountered in large wounds of the heart and in the phenomena of missile embolism.

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Technician, Fourth-Grade Walter Meigs, Jr., was kind enough to prepare the illustrations used herein.

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FRACTURES OF THE ACETABULUM:
The Nature of the Traumatic Lesions, Treatment, And Two-Year End-Results

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THIS IS THE SECOND OF A SERIES of three papers concerned with the analysis of 58 injuries of the hip joint which occurred in jeep accidents in World War II in the European Theatre of Operations. A previous paper has been concerned with dislocations of the hip joint.[50] The present paper deals with fractures of the acetabulum without dislocation. A following paper will deal with fracture-dislocations. The mechanism of injury in each group of cases, as determined from the case history and by the circumstantial evidence from associated injuries in the ipsilateral extremity, was the same with few exceptions. The fracture of the acetabulum was a first-stage or incomplete "dashboard type" fracture-dislocation. In all of these injuries the fractures create incongruity of the joint surfaces, which is the first consideration in treatment. Damage to vascular structures of the joint capsule are assumed to occur only in dislocations and fracture-dislocations. The development of late complications, including the role of mechanical and vascular factors, are to be discussed by means of a comparative analysis of a two-year follow-up study of all types of cases in the final paper.[51]

The 16 cases of fractures of the acetabulum (Table I) to be presented in this communication fall into the following classifications:

Fracture of the rim of the acetabulum, five cases (three of the superior and two of the posterior rim).

Central fracture, eight cases (seven fractures of the body of the pubis and inner table of the pelvis, one fracture of the anterior rim and superior ramus of the pubis with intrapelvic protrusion of the head of the femur).

Comminuted or bursting fractures disorganizing the entire joint cavity, three cases.

This division of cases fits in with many of the well-known textbook classifications.[6] It differs from the purely morphologic classifications in that it is not entirely theoretical, but based upon the morbid and roentgenologic anatomy of the region, upon present knowledge of the localization of function of various parts of the acetabulum, and upon the problems of treatment. It will be shown here and later[51] that fractures which destroy a significant part of the superior and posterior rims of the acetabulum require open operation. Fractures limited to the anterior portion of the articular surfaces require only conservative treatment by means of traction. More extensive fractures which destroy the entire joint surface do not respond well to any form of treatment

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TABLE I.—*Fractures of the Acetabulum in Military Personnel*

Weight-

TABLE I.—*Fractures of the Acetabulum in Military Personnel*

Case No.	Age	Other Injuries of Ipsilateral Extremity	X-ray	Treatment	Weight-bearing (months)	Complications	Two-year Follow-up
16	21	Lacerated wound thigh, leg, knee	Undisplaced fracture superior rim	Traction 8 weeks	3	None	Normal hip, Slight pain
17	20	.....	Slightly displaced fracture superior rim	Traction 8 weeks	4	None	Pain and difficulty standing long periods
18	32	Hemarthrosis. Lacerated wound knee	Displaced fracture superior rim	Open reduction, internal fixation	5	None	Normal hip occasional mild joint pains
19	29	Pott's fracture	Widely displaced fracture posterior and inferior rims	Traction 8 weeks Fracture unreduced	4	Treatment neglected in enemy hospital for 2 months	Snapping hip, severe pain, slight limitation of motion
20	20	Fracture patella	Widely displaced fracture posterior and inferior rims	Traction 8 weeks Fracture unreduced	Not known	Not known	No follow-up
21	35	.....	Undisplaced central fracture	Traction 6 weeks	6	None	Normal joint
22	24	.....	Undisplaced central fracture	Bed rest 3 weeks	3	None	Normal motion of joint, slight pain and clicking
23	26	Severe contusion knee	Undisplaced central fracture	Traction 8 weeks	Not known	Not known	No follow-up
24	21	Lacerated wound knee	Undisplaced central fracture	Traction 8 weeks	3	None	Normal motion. Slight pain. Unable to lift heavy objects
25	42	.....	Displaced central fracture	Traction 8 weeks	5	None	Normal hip
26	22	Fracture patella	Displaced central fracture	Traction 8 weeks	6	None	Normal motion, joint pains, difficulty standing long periods
27	29	.....	Displaced central fracture	Traction 8 weeks	Not known	None	No follow-up
28	39	.....	Central fracture, body and descending ramus of pubis, intrapelvic protrusion of head	Lateral and longitudinal traction 8 weeks	4	None	No follow-up
29	29	Fracture midshaft femur	Cominuted fracture, displacement of all parts and superior and posterior rims	Traction 8 weeks	9	Injury kidney, persistent hematuria	Severe pain, ankylosis
30	25	Compound fracture upper third femur	Comminuted fracture, displacement of all parts and superior and posterior rims	Traction 12 weeks	18	Injury kidney, persistent hematuria	Severe pain, ankylosis
31	32	.....	Comminuted fracture, displacement of all parts and superior and posterior rims, multiple fractures pelvic ring bilaterally	Traction 12 weeks	4	Laceration posterior urethra. Suprapubic cystostomy. Crushing injury and extirpation of the testicle	Severe pain, ankylosis

and usually result in great disability, frequently with associated ankylosis and degenerative arthritis.

THE TRAUMATIC LESION

For intelligent evaluation and treatment of fractures of the acetabulum, certain important anatomic considerations must be clearly understood. The weight-bearing surface of the acetabulum consists of a lunate or horse-shoe-shaped platform of bone covered with articular cartilage. The anterior portion of the horseshoe, which is formed from the body of the pubis, is approximately half as wide as the superior portion. The anterior rim may be excised, as in arthroplastic operations, without seriously altering the function of the joint, but the posterior rim is necessary for stability. The superior shelving portion, which is the thickest portion of the innominate bone, is vital for the weight-bearing function of the acetabulum.

Fractures of the posterior rim of the acetabulum of various magnitudes, and involving various portions of its lunate articular surfaces, are not uncommon, and have frequently been observed and repaired. Fractures of the superior rim are extremely uncommon, presumably because of the volume of the bone and the adaptation of the stress lines of the trabeculae in this region to the burden of the weight of almost the entire torso.[54] In one case of superior rim fracture in this series (case 18), at open operation the fragment contained 0.5 cm. of the width of the articular cartilage, and the entire iliofemoral ligament was attached to the outer cortex of the rim of the fragment.

Fractures of the central portion of the acetabulum in this series showed an infinite number of patterns and various degrees of displacement. The variety associated with intrapelvic protrusion of the head of the femur has received the attention of many writers since 1788 when the lesion was described by Callisen and later provocatively termed "central dislocation" by Krönlèin in 1882.[10] By 1928, with the new impetus from roentgen-ray methods of diagnosis, there were 138 cases of these rare injuries reported in the literature. Although many more cases have been reported since then, there are still great gaps in our knowledge of the traumatic lesion due to the inadequacy of routine roentgen-ray examinations, the lack of necropsy studies, and the infrequency with which the fracture has been seen at open operation.[36] Additional case reports continue to be important for information in proper selection of the cases for different types of treatment, and for data on the end-results. Most of the cases in the literature, like the cases reportd in this series, were only partial protrusion and not the highly comminuted bursting type of fracture which is almost irreparable. A few of the cases illustrated in the literature are fractures of the body of the ischium and the triradiate seam of the acetabulum associated with a second fracture of the superior ramus of the ischium, but not much intra-pelvic protrusion was possible under these conditions.[55] In the majority of cases, whe. the head protrudes into the pelvis, there is a fracture of the anterior rim and the body of the pubis associated with a second fracture of the superior ramus of the pubis upon which the displacement of

the inner table of the pelvis hinges. The head of the femur escapes into the fracture site, which is the anterior portion of the acetabulum, and the vital superior and posterior lunate cartilages escape relatively unharmed. Usually the head is easy to draw out of the fracture site and replace in normal apposition to the horse-shoe-shaped cartilage and it can be held there by traction for

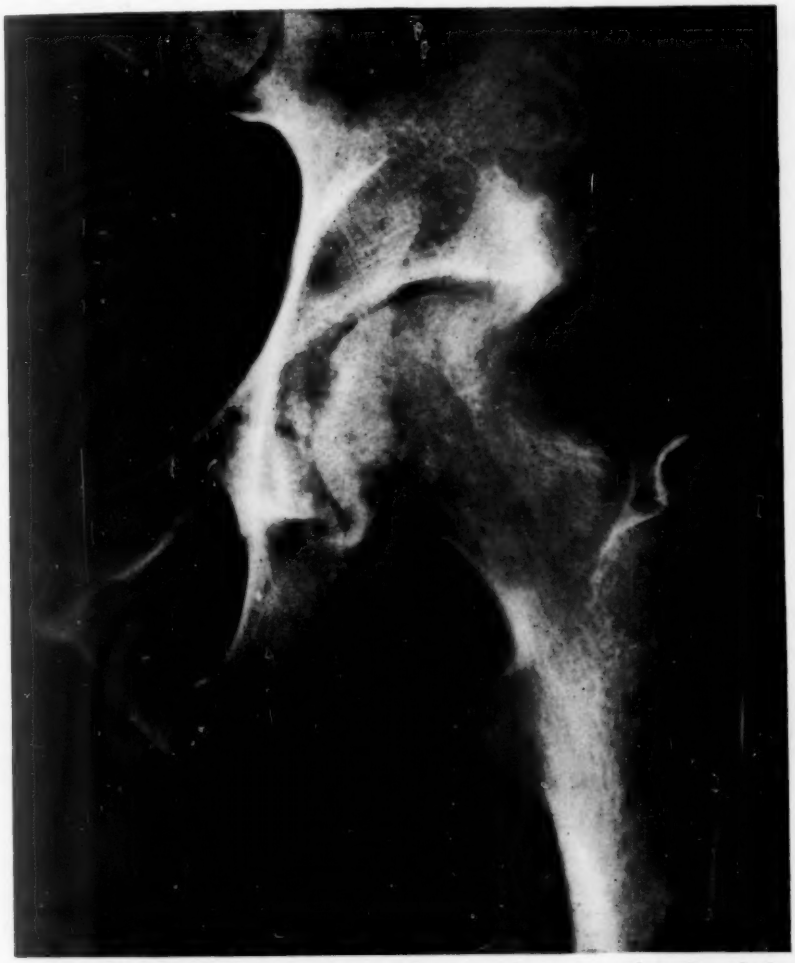


FIG. 1-A.—Roentgenogram of a fracture of the posterior rim of the acetabulum on the day of the injury as seen in the anteroposterior view. The displacement of the fracture was not considered significant by this examination. (Case 19)

eight weeks or until healing occurs. The inner table of the pelvis remains displaced, but the anterior portion of the joint and the fracture site fill in with callus and are repaired by formation of new bone and fibrocartilage.

FRACTURES OF THE RIM OF THE ACETABULUM

The three cases of fracture of the superior rim and the two cases of fracture of the posterior rim of the acetabulum in this series were diagnosed by

emergency roentgenograms taken in field and evacuation hospitals. The patients were immobilized in hip spicas in 30° abduction, 20° flexion and neutral rotation and were transported without further treatment.

Conservative Treatment. The degree of displacement and the size of the rim fragment determined the type of treatment for each case. Re-examination with more elaborate roentgen-ray equipment in fixed general hospitals in the communication zone, including posterio-oblique views, revealed undisplaced

FIG. 1-B.—Roentgenogram of the same case as illustrated in Figure 1-A, six weeks after the injury as seen in the posterior oblique view. This view demonstrates the displacement of the fracture. When the hip was examined in flexion in this case, little more than half of the original lunate cartilage of the acetabulum articulated with the head of the femur, but the joint was stable.

or very slightly displaced fractures in two cases, and displaced fractures in three cases. In one case the displacement was not appreciated until six weeks after the injury because of the failure to examine the fracture in the important posterior-oblique views (Case 19, Fig. 1). In another displaced fracture (Case No. 20) operative treatment was contraindicated because of severe

chest and head injuries. All of these cases were treated conservatively in traction-suspension for periods varying from three to eight weeks, depending upon the extent of the lesion, except one fracture of the superior rim (Case No. 18) which is reported in detail below.

Surgical Treatment. Because of the involvement of a vital portion of the acetabulum, Case 18 was treated immediately by open reduction and internal fixation. The hip joint was exposed by the anterior iliofemoral approach, exposing the joint capsule in the sulcus between the sartorius, the tensor fascia

FIG. 2-A.—Preoperative roentgenogram showing fracture of the superior-posterior rim of the acetabulum (Case 18).

femoris, and the rectus femoris. After irrigation and curettage to remove all the blood obscuring fracture lines, the main fragment was replaced in anatomic position with its attachments to capsule and anterior iliofemoral ligament intact. Although the fracture was clearly visible by this approach, a transfixing screw could not be inserted at right angles to the fracture site. This was accomplished by a lateral stab wound in the gluteus medius large enough to permit the introduction of a long drill point screw driver at right angles to the middle of the fracture line. The fragment dovetailed and was compressed so accurately into place that the fracture line was hardly visible in the postoperative roentgenogram. (Fig. 2). Fractures of the superior rim, the strongest portion of the acetabulum, are rare,[54] and a case similar to this one has not come to our attention in the literature.

Fractures of the posterior rim of the acetabulum are more common and are easily repaired by the posterior approaches which we have used with the same success as many others in recent years.[51]

CENTRAL FRACTURES OF THE ACETABULUM

The eight fractures of the acetabulum in this series (Table I) in which the rim of the acetabulum was largely intact and the head remained in the joint cavity are classified as central fractures. In four instances there was no displacement. In three instances there were fractures of the dome of the acetabulum with displacement of the inner table of the pelvis for a distance of about the width of the cortex. One case (Case 28) represented the typical fracture of the anterior acetabulum and the body of the pubis with intrapelvic protrusion of the head of the femur and wide displacement of the inner table of the pelvis. The patients were immobilized in a Thomas splint or a spica, with the joint in neutral position and were evacuated from the combat zone without manipulation or other treatment.

FIG. 2-B. — Roentgenogram showing anatomical repair of the joint surface and internal fixation of the fracture, one week postoperative (Case 18). The screw should penetrate the inner table of the pelvis to obtain reliable immobilization of the fragment.

Conservative Treatment. On their arrival in general hospitals in the communication zone after further roentgenologic studies, all the patients were suspended in skeletal traction for six to eight weeks. In the case of intrapelvic protrusion of the head of the femur (Case 28), reduction was accomplished by the use of a trochanteric vertical Kirschner wire placed just inside the lateral cortex. The head of the femur was manually pulled out into normal relationship with the rim of the acetabulum by the use of the large size wire-tautening bow for a handle. The hip was suspended in a Balkan frame for eight weeks with five pounds' lateral traction and ten pounds' bilateral longitudinal skin traction through the lower extremities. The ipsilateral side of the bed was elevated slightly for lateral countertraction. Although the displacement of the inner table of the cortex was not modified by this treatment, the fracture site filled in with abundant callus within the four months that the

patient was under observation. The failure of the fracture site to follow after the extracted femoral head is similar to the observations made in the civilian cases reviewed (Table II) and is apparent in the "before and after" pictures of almost every case reported in the literature (Fig. 3).

EXTENSIVE COMMINUTED FRACTURES OF THE ENTIRE ACETABULUM

In the three cases in this series (cases 29, 30 and 31) in which comminuted fractures involved all portions of the acetabulum, the joint was disorganized and incongruent. In two of the three patients in the group there was an associated fracture of the ipsilateral femur.

Emergency management was limited to prophylactic treatment for shock. The patients were immobilized in hip spicas in slight abduction and were immediately evacuated from the combat zone.

Conservative Treatment. All three patients were treated conservatively in traction. Skeletal traction by means of a Kirschner wire through the supracondylar region aligned the fractures of the shaft of the femur but had little effect upon the fractures of the acetabulum. It was assumed from the beginning in these cases that arthroplasty or fusion of the joint would be necessary at a later date.

FOLLOW-UP STUDIES

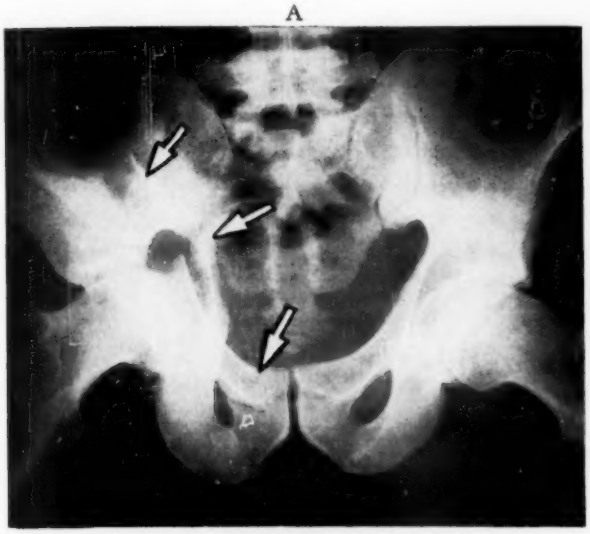
The status of 14 of the 16 patients in this group could be determined at the end of two years by means of personal letters from them or from their physicians, by reports of examinations in United States Army hospitals, and, occasionally, by firsthand observation. Unfortunately, it was not possible to locate the single patient with intrapelvic protrusion of the head of the femur. The results of fractures of the acetabulum in military personnel are to be compared with similar fractures in a group of patients, including two similar cases of intrapelvic protrusion, from the Fracture Service of the Massachusetts General Hospital (Table II).

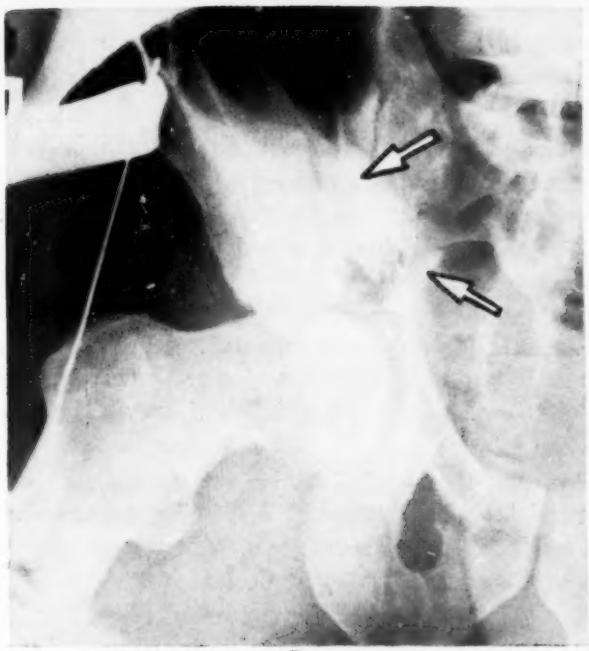
At the end of two years, 11 of the 14 military patients followed had no serious disability. Many, however, complained of mild pain, snapping or clicking sensations in the joint, stiffness early in the morning, and discomfort from lifting heavy objects. Patients with displaced fractures of the supero-posterior rim of the acetabulum appeared to have more symptoms and more disability than those with anterior rim or central fractures. One patient (Case 19) with an unreduced fracture of the posterior rim had severe pain and some limitation of motion at the extremes of the normal range in all directions. One patient (case 18), whose joint was accurately repaired at open operation, in contrast, had a normal hip. In both these cases the displaced fragment of the rim was relatively large. If the fragments were smaller or thinner and carried less of the articular cartilage with them, the important function of the joint would probably not be affected, regardless of whether or not they were replaced. The three patients with extensive fractures of the acetabulum and destruction of the joint cavity had ankylosis and complete disability two years after the injury.

TABLE II.—*Selected Fractures of the Acetabulum at the Massachusetts General Hospital 1932 to 1946*

Unit No.	Age	X-ray	Treatment	Weight-bearing (months)	Follow-up
493496	14	Central fracture, slightly displaced	Traction 4 weeks	2	Normal hip at 2 years
78702	60	Central fracture, slightly displaced	Traction 4 weeks	3	Normal function at 2 years but tires easily because of mild pain
345913	64	Central fractures, medial displacement body of pubis and anterior acetabulum	Bed rest	3	Moderately painful hip, narrowing of joint space in X-ray
320953	50	Central fractures, medial displacement body of pubis and anterior acetabulum	Bed rest	3	No symptoms at 1 year
514457	40	Central fractures, medial displacement body of pubis and anterior acetabulum, intrapelvic protrusion of head of femur	Lateral and lungitudinal traction, 4 weeks	3	Normal function, slight limitation of flexion at 1 year
353469	22	Central fractures, medial displacement body of pubis and anterior acetabulum, intrapelvic protrusion of head of femur	Traction	3	Normal function, slight limitation of flexion at 3 years
537224	52	Central fracture, comminuted, bursting type	Open reduction 12	12	Painful hip, moderate ankylosis at 1 year

A





B

FIG. 3-A.—Roentgenogram showing central fracture of the acetabulum with intrapelvic displacement of the anterior rim of the acetabulum and the inner table of the pelvis. The displacement hinges on the fracture of the superior ramus of the pubis indicated by the lower arrow (Case 28). Other arrows indicate the main fragments.

FIG. 3-B.—Roentgenogram of the fracture in Figure 3-A showing the head of the femur withdrawn from the fracture site by lateral skeletal traction through a vertical Kirschner wire in the greater trochanter. The main fragments of the fracture do not follow the head in this type of fracture (Case 28).

In two of the seven fractures of the acetabulum studied from the fracture service of the Massachusetts General Hospital (Table II), the head of the femur protruded into the pelvic cavity, and roentgenograms showed the typical features of displaced fractures of the body of the pubis and the internal table of the pelvis. Treatment was the same as in case 28 of the military series, and in neither instance was there any disability at the end of one and three years respectively. It is difficult to understand, in this type of central fracture, why even when there is intrapelvic protrusion of the head of the femur, healing occurs without functional disability, regardless of the displacement of the inner table of the pelvis. The explanation may be that the fractures in these cases affect the anterior rim, a nonessential part of the joint, and that the vital posterior and superior portions of the horseshoe-shaped articular cartilage are spared. When, on the other hand, intrapelvic protrusion of the head of the femur is associated with extensive fractures of the acetabulum and bursting of the triradiate seam of illium, ischium and pubis, or with distortion of the rim of the acetabulum, the functional result is very poor. The division of the cases of central fractures into these two categories would explain the discrepancy in results[1, 3, 5, 19, 27, 31, 32, 37, 43, 45, 58] reported in the literature for the treatment of this type of acetabular fracture.

DISCUSSION

The experience gained in the treatment of the cases reported in this paper supports the impression received from a survey of the literature that the seriousness of a fracture of the acetabulum depends upon whether the superior and posterior portions of the lunate articular cartilage are defective. Open reduction has been advocated[6, 13, 32, 37, 57] for rim fractures in recent years, the principle being that reposition of the joint fragments is as necessary in the hip as in injuries of other weight-bearing joints. Previously, many writers accepted the imperfect results of conservative treatment because of the formidable nature of operative treatment and lack of knowledge of late degenerative changes in the joints.

Central fractures of the acetabulum, including cases with intrapelvic protrusion of the head have been generally considered together and treated as one problem in various ways. The cases with intrapelvic protrusion of the head of the femur have excited a great deal of interest and there are now many isolated case reports upon which present methods of treatment are well-established. It is not unusual that these injuries should occur in jeep accidents. The lesion can be produced experimentally and accidentally by a blow on the flexed knee transmitted to the head of the femur[47] and possibly even by indirect forces of abnormal muscle action during convulsions from shock therapy.[22] More commonly, it is incurred by a blow on the greater trochanter. Variations in the pattern of the lesion and possible inclusion of various parts of the rim of the acetabulum, may be determined by the degree of abduction of the limb and the amount of internal and external rotation of the head of the femur. If it is in external rotation, a blow on the greater trochanter would drive the

head of the femur into the anterior portion of the acetabulum where intrapelvic protrusion is possible with minimum damage to the weight-bearing lunate-shaped articular cartilage.

Satisfactory results have been reported by the use of a variety of systems of treatment capable of extracting the head of the femur from the pelvis. One of the earliest methods reported to give uniformly satisfactory results was the abduction spica of Whitman, in which the greater trochanter is used as the fulcrum.[8, 17, 23, 25, 29, 48, 56] The favorite among the more modern technics is lateral or combined lateral and longitudinal traction. Slings or pressure pads applied to the medial aspect of the upper thigh[26, 39, 41, 42, 53] and the Jahss cast[35] have been employed for lateral traction, but skeletal traction obtained through a trochanteric screw[14, 33, 34, 44] or a Kirschner wire[18, 24, 40] or a Steinman pin[38] is more comfortable for the patient. Self-retained traction devices with a Thomas-Jones abduction splint,[4] a windowed hip spica,[34, 46] or Hoke's apparatus[49] facilitates the nursing care.

All of these methods have proved capable of retaining the normal position of the head of the femur on the lunate articular cartilage of the acetabulum until the fracture heals. On the other hand, the "before and after" roentgenograms of almost all of the cases reported in the literature show, as in the cases reported herewith, that the displaced inner table of the pelvis seldom, if ever, follows the head of the femur when it is drawn out of the fracture site. It has been reported that the fracture can be modified by manipulation through the rectum,[9, 15, 26] but the results are not striking and the method is discouraged by some surgeons.[28] Open reduction is practical in very severe cases through an anterior iliofemoral approach, exposing the true pelvis. Engel[16] repaired the roof of the acetabulum by this method, tapping the bone flap of the inner table into place with a bone set and wooden mallet. Levine[35] reduced an unusually large fragment of bone and applied a steel plate held in place by four screws along the anterior pelvic rim. Open operations are also described by Lexer,[36] and Konig.[30]

It is difficult to evaluate the results reported in both the old[21, 52] and the new[11, 20, 57, 58] literature, because exact limits of the injury are not frequently clearly described. The author's illustrations suggest, however, that the poorest results were secured in cases in which the rim of the acetabulum was involved and the joint cavity was left permanently incongruous and enlarged in depth and width. Good functional results were usually reported in the cases in which displacement was limited to a large single fragment of the body of the pubis and the inner table of the pelvis and in which the head of the femur was dislocated into the fracture site.[3, 20, 27] In such cases the anterior acetabular fossa regenerates by abundant callus and fibrocartilage, which readily grow across the fracture site in this highly vascular portion of the skeleton.

The true incidence of degenerative or traumatic arthritis and the late results of these and other types of injuries of the acetabulum are known only in isolated, poorly documented cases which come to the attention of the

surgeon many years after the injury. Complete avascular necrosis seems to have been reported in one case, two to three years after an injury in which the head of the femur was virtually locked in the fracture site,[14] and two other severe cases[2, 7] in which one might assume ischemia of the capsula reflexa was the cause.

SUMMARY

1. Sixteen cases of fractures of the acetabulum which occurred in military personnel and seven similar cases, which were studied on the Fracture Service of the Massachusetts General Hospital, are reported.

2. Fractures of the superior and posterior rims of the acetabulum of significant magnitude almost always resulted in some disability, but good function of the joint was obtained in one case after open reduction and accurate internal fixation.

3. Central fractures of the acetabulum can be classified in two groups, according to various roentgenogram patterns of the traumatic lesion and the functional results achieved at the end of two years. A. Central fractures limited to the pubic portion of the acetabulum and the descending ramus of the pubis, even with intrapelvic protrusion of the head, responded well to conservative treatment and showed an excellent functional result after one to three years. B. Central fractures bursting the triradiate line of the acetabulum were impossible to reduce by conservative methods and resulted in great disability. Fusion or arthroplasty was advised in three such cases after two years.

4. The differences in end-results can be explained on the basis of cumulative, experimental, operative, and roentgenologic observations, as well as by end-results. All the evidence is to the effect that fractures of the pubic portion of the acetabulum are chiefly lesions of the anterior rim, which is not essential to the function of the hip joint while, on the other hand, stellate or bursting fractures involve or distort the lunate superior and posterior articular cartilage of the acetabulum which is necessary for normal weight-bearing.

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EXPERIMENTAL STUDIES OF ALGINATES AS HEMOSTATICS*

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THE THREE ABSORBABLE hemostatic packing materials which have had extended trial in clinical surgery are, in order of their introduction, human fibrin foam, oxidized cellulose—in the form of gauze or cotton—and gelatin sponge. There are minor differences in the immediate hemostatic effect of these different materials and in the technics of their surgical use, but they are all non-irritating in the tissue, non-toxic and absorbable. None of these can be sterilized by autoclave, and should a material be developed which had this advantage and also the desirable properties of the other agents it would be a welcome addition to our surgical armamentarium.

It was suggested that alginic acid or its salts might answer this purpose. Alginic acid is a naturally occurring organic acid derived from seaweed (Laminaria digitata) with a formula closely resembling cellulose.[1] The alginates had already been developed for wide commercial usage. Woven and spun preparations, gauze and stockinette were available. As is often the case with what is thought to be an original idea, independent investigations were undertaken in several different laboratories. The credit for the first experimental observations goes to Blaine, of England, whose paper, although not published until January 1947, was submitted to this journal for publication in January 1946.[1]

Our own studies began about that time and we were accelerated because we had the privilege of reading Major Blaine's article in manuscript. As he says in his text, "Exigencies of the service in wartime have made it impossible to conduct a more complete examination of the many problems at issue. It has been shown, however, that alginates possess certain properties which make their surgical use attractive." There was no doubt in our minds, therefore, that the alginates held considerable promise. We had hoped to obtain directly from Major Blaine some of the alginate gauze he had employed in his studies for comparison with that submitted to us by the chemists who had suggested its possible surgical application, comparison particularly in regard to texture and tensile strength. We also planned to run a comparative series of experiments on oxidized cellulose and this new material, with especial reference to the immediate effective hemostatic properties of each agent, and the tissue reactions. Somewhat later it seemed imperative that the pharmacology of the alginates should be studied in detail for comparison with oxidized cellulose and this was undertaken by another group of investigators.[2] Stimulus was also given to this study by the publication of a letter to the editor in Science, May 1946, in which Smith[3] reported the styptic action of local application of

* The work described in this paper was done under a grant from Johnson & Johnson, New Brunswick, N. J.

alginic acid powder in 100 cases of tooth extraction and minor oral surgery. The dose would obviously be small in these cases and presumably most of the wounds were open.

The alginates submitted to us by the Research Laboratories of Johnson and Johnson were processed in an effort to maintain tensile strength and achieve ease of handling in actual surgical manipulation. Early samples of varying calcium content were submitted, and in addition, a sizing agent as well as a buffering solution were sometimes used. The chemical analysis shown in Table I makes it clear that variations in tissue reaction could therefore be attributed to a number of factors.*

With all samples it was observed that the tensile strength was not as good as that of oxidized cellulose, and that the combination of the material with citrated blood resulted in a soft, brownish-black, mushy paste more difficult to handle with forceps than the black gelatinous mass so formed with oxidized cellulose. It was expected, however, that if other features were satisfactory, minor changes in preparation might alter these physical properties. The

* METHOD OF PREPARATION

Calcium Alginate Gauze:

31B, 35A, 35C	—	Treatment: 15 minutes in HCL, pH 1.5. Washed, buffered, 15 minutes, washed, air-dried.

100 (4) Denier Calcium Alginate Stockinette:

62D1, 69	—	Treatment: Washed in water. Extracted with ethyl alcohol and ether (separately), treated in HCL (0.974N) 1 hour, washed and treated 2 hours in an excess of 0.2N $CaCL_2$, washed. Buffered, air-dried.
73		Treatment: Similar to 62D1 and 69 but not buffered. Washed with tap water, pH 7.4, dried at 45°.
62B1, 65	—	Treatment: Washed in water. Extracted as 62D1 and 69, treated overnight in 0.974 N HCL, and washed CL free. Buffered, washed, air-dried.
64	—	Treatment: Approximately normal HCL 1 hour. Washed once and treated in an equal quantity of fresh acid 30 minutes. Washed. Buffered 20 minutes. Washed, air-dried.
41-116	—	Treatment: Dilute HCL until calcium content reduced to 0.15%. Buffered.
41-118	—	Treatment: Similar to 41-116 but alcohol-ether extracted to remove Fixanol.
41-120	—	Treatment: Warm water (40° C.) Calcium content reduced with dilute HCL (3% then 1%). Washed with cold water. Dried at 60°.
41 151	—	Treatment: Extracted with acetic acid to remove Fixanol. Dilute HCL to remove calcium. Alginic acid thus derived oxidized with HIO_4, with partial conversion of the secondary alcohol groups to aldehyde groups. Treated with dilute HNO_3, air-dried.
41-152	—	Treatment: Similar to 41-151 but Fixanol not extracted.
89-31, 89-32	—	Treatment: Fuming HNO_3 at room conditions 1 hour. Washed free of acid, air-dried.

affinity of the alginic acid for hemoglobin as demonstrated by the laked blood test was similar to that of oxidized cellulose.

In our earlier studies of oxidized cellulose[4, 5] one of the standard tests was solubility in 0.15 Molar solution of sodium bicarbonate. Satisfactory preparations of oxidized gauze and oxidized cotton dissolve completely without residue. No animal tests were undertaken on samples which showed re-

TABLE I.—*Alginates Tested*

Lot No.	Weave	% Free COOH	% Ca	Buffered* %K	Nitrated %N	Fixanol† Sizing	Sterilization
31B	Gauze	22.14	3.03	Approx. 2.5	..	+	Steam
35A	"	"	2.45	"	..	+	"
35C	"	"	3.06	"	..	+	"
62D1	Stockinette	"	2.80	"	..	0	"
69	"	"	1.82	"	..	0	"
73	"	"	2.81	0	..	0	"
62B1	"	"	0.25	"	..	0	"
65	"	"	0.58	"	..	0	"
64	"	"	0.19	"	..	+	"
41-116	"	"	0.10	Analyzed 2.54	..	2%	"
41-118	"	"	0.10	"	..	0	"
41-120	"	"	0.10	Approx. 2.5	..	+	"
41-151	"	"	0.0	..	0.2	0	Formaldehyde 0.11 res.
41-152	"	"	"	..	0.3	2%	"
89-31	"	16.3	"	0.0	4.0	Trace	Formaldehyde
89-32	"	14.6	"	"	4.68	"	"

*Potassium acid phthalate solution 0.05 Molar pH 4.0
†Sizing: Fixanol—octyl pyridium bromide. A finishing agent used in the manufacture of alginate yarn to prevent sticking together of the monofilaments.

TABLE II.—*Standard Rat Tests on Calcium Alginate Gauze*

Lot No.	% of Ca Content	No. of Animals	Days Post-Op.	Absorbed	Inflammation	Fibrosis	Conclusions
31B	3.03	5	2—28	0	2+	1+	Unsatis.
35A	2.45	5	7—21	0	1+	1+	Unsatis.
35C	3.06	5	7—21	0	2+	1+	Unsatis.
62dl	2.80	4	4&7	0—±	Contam.	Contam.	Repeat*
69	1.82	6	2—7	±	1+	2+	Unsatis.
73	2.81	5	2—7	±	±	±	*Also unsatis.
62Bl	0.25	6	7	Completely	0	0	Satis.
64	0.19	6	2	Completely	Min.	..	Satis.
65	0.58	4	2	Completely	Min.	..	Satis.

sidual fibers of material. In applying this test to calcium alginate it also was found to be soluble in 0.15 Molar $NaHCO_3$, but there was a precipitate of calcium carbonate which was not to be confused with insoluble residue. All samples tested were completely soluble.

Affinity for hemoglobin, and solubility tests having borne out the expectation that alginic and cellulosic acid were somewhat similar in behaviour as

well as structure, tests for tissue reaction were then undertaken. The first tests were for absorption and tissue response and were conducted according to the technic devised by Lattes Frantz.[6] This was reported in this Journal in 1945. It consists of aseptic implantation of materials under scrutiny in the subcutaneous tissues of the back of rats. In our own previous studies, fibrin foam, gelatin sponge, oxidized cellulose and a large number of other substances had been subjected to this "rat test." Only the first three were found to be

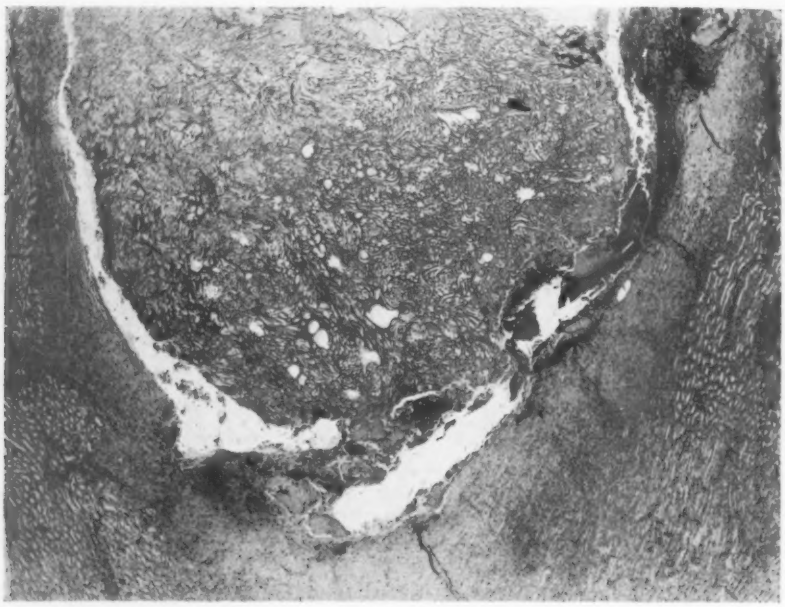

FIG. 1.—S. P. 25509. Photomicrograph, X38, of di-aldehyde alginic acid gauze (41-151) in experimental wound of upper pole of kidney. Dog —42 days. Large amount of unabsorbed material. A broad zone of fibrous scar tissue separates kidney parenchyma from the hemostatic packing. On higher magnification this tissue is seen to contain many hemosiderin laden phagocytes. There are no polymorphonuclear leukocytes and no foreign body giant cells.

both non-irritating and completely absorbed. In testing the alginic acid preparations by this method it was thought unnecessary to run simultaneous controls of oxidized cellulose since detailed studies had already been reported (4 and 5) and the techniques used were the same. The results of the first series of rat tests are shown in Table II.

These early promising samples (62B1, 65 and 64) led us to study the effectiveness of the new materials in experimental hemorrhage. It will be seen from Table II that the unsatisfactory samples were those of higher calcium content, and the trials of hemostasis were accordingly made on approximate duplicates of 62B1, but with even lower calcium content (41-116, 41-118 and 41-120). Again the tests employed were those by which oxidized cellulose had originally been studied and which have been reported in detail (4

and 5), i.e. wounds of kidney and spleen. Immediate hemostatic effect in an experimental or clinical wound is obviously not subject to exact measurement. The wounds of the kidney in this technique are made as nearly comparable as possible, one in the upper and one in the lower pole. The capsule is incised, a clamp is thrust into the parenchyma and spread so that brisk bleeding ensues. The wound is then lightly packed with the hemostatic agent to be studied. It was in such wounds that we first observed that oxidized gauze

FIG. 2.—S. P. 25509. Photomicrograph, X38, of control mound, lower pole of same kidney as Fig 1, packed with oxidized cellulose. The foreign body in the capsule is the markingsilk suture. No gauze is seen. The site of the implant at this magnification is characterized by diffuse dark staining. There isc no unabsorbed material. In higher magnification this zone is almost entirely composed of phagocytes, some hemosiderin laden. The bulk show the basophilic staining characteristic of cellular reaction to oxidized cellulose. There is almost no scar tissue except the linear extension of the wound seen at the base on the right, and slight fibrous prolif eration in the capsule.

had a specific hemostatic effect. Hemorrhage was more rapidly controlled with this gauze than with plain gauze. The alginate preparations when compared with oxidized cellulose exhibited very little hemostatic effect. The hemorrhage was controlled in these standard kidney wounds chiefly by the presence of packing and not by any evident styptic action.

Further confirmation of this was obtained in standard tests in shallow surface defects in the spleen where the packing effect is absent. Here little styptic action of alginate was noted, although the preparation without sizing was somewhat more effective than those with it. Controls here were also made with oxidized gauze. (Table III).

TABLE III.—*Comparative Studies in Experimental Hemostasis and Tissue Reactions in Dogs with Oxidized Cellulose and Alginic Acid*

	Lot No.	Chemical Analysis	Autopsy Days Post-Op.	Immediate Hemostatic Effect in Spleen and Kidney		Tissue Reactions in Kidney: Absorption		Tissue Reactions in Kidney: Evidence of Inflammation		Comment
				Alg.	Ox. Cell.	Alg.	Ox. Cell.	Alg.	Ox. Cell.	
1.	41–116 (Chenoweth B)	Buffered Sizing Ca 0.1%	17	1+	4+	3+	4+	3+	0	Progressive downhill course.
2.	41–116	"	40	±	4+	2+	4+	3+	0	Sick for 6 days post-op.
3.	41–118	Buffered. No sizing Ca 0.1%	4	2+	4+	0	0	3+	3+	Peritonitis. No culture.
4.	41–118	"	28	2+	4+	2+	4+	1+	0	Sick for 5 days post-op.
5.	41–120	Not buffered No sizing Ca 0.1%	28	±	4+	4+	4+	3+	0	Very sick for 5 days post-op.
6.	41–120	"	40	±	4+	2+	4+	3+	0	Loss of weight and strength throughout
7.	41–151 (Chenoweth C)	Di-aldehyde No sizing Ca 0%	42	2+	4+	2+ (Fig. 1)	4+ (Fig. 2)	1+	0	Poor health throughout post-op course.
8.	41–152 (Chenoweth C)	Di-aldehyde Sizing Ca 0%	7	±	4+	±	±	2+	1+	Died. Antemortem clot, rt. auricle.

As the immediate hemostatic effect of the alginates did not compare favorably with that of oxidized cellulose, further chemical modifications of the preparations was proposed in order to improve this property. One of these new preparations was the di-aldehyde of alginic acid (41-151 and 41-152) and this was moderately effective in immediate hemostasis. (Table III). It was not a promising modification, however, because the material, originally proposed to facilitate sterilization, no longer had the advantage of being sufficiently heat resistant to be sterilized by autoclave. Another preparation suggested, nitrated sodium alginate, was also too unstable for autoclave. In spite

TABLE IV.—*Standard Rat Tests on Recent Preparations*

Lot No.	Description	No. of Animals	Days Post-Op.	Absorbed	Inflammation	Fibrosis	Conclusion
41-120	Alginic acid. Not buffered. No sizing Ca 0.1%	5	2—8	Completely	Variable	1+	Unsatis.
41-151 (Chenoweth C)	Di-aldehyde No sizing Ca 0%	5	2	Completely	0	0	Satis.
41-152 (Chenoweth C)	Di-aldehyde Sizing Ca 0%	5	2	Completely	0	0	Satis.
89-31 (Chenoweth D)	Nitrated sodium alginate with sizing	4	1—7	Completely	1+	0	Toxic*
89-32 (Chenoweth D)	Nitrated sodium alginate with sizing	4	2—5	Completely	±	0	Toxic†

*1 Death—24 hours. 2 Animals lethargic until sacrificed.
†3 Deaths—2, 2 and 5 days. 1 Animal lethargic when sacrificed at 3 days.

of this disadvantage a second short series of rat tests was undertaken as a preliminary to possible further studies on hemostasis. The results are shown in Table IV. At the time these tests were made we were apprised of the observations of Chenoweth on the toxicity of the material in cats.[2] Detailed autopsy studies were not attempted on the rats in this last series because postmortem changes were often advanced, and there were further depredations by cage mates. In comparison, however, with several hundred previous rat tests the morbidity and mortality rate in this group was considered significant.

With this knowledge, a careful re-reading of Blaine's article led us to the belief that although the cats he subjected to liver lacerations had survived when the bleeding had been controlled with alginates, there had been early toxic effects comparable to those reported by Chenoweth. Moreover, the polymorphonuclear leukocytic response which the author described in the local tissue reactions, had been duplicated in many of our own observations, and indicated a greater degree of irritation caused by the alginates than by oxidized cellulose.

SUMMARY AND CONCLUSIONS

1. Local tissue reaction to various spun and woven preparations of alginic acid and its derivatives have been studied in a series of rat tests. Although some of the preparations evoked a minimal inflammatory response, several were apparently irritating and engendered a considerable fibrous tissue replacement when finally absorbed. The most favorable preparations were slightly more irritating than oxidized cellulose. That they were also toxic even when introduced thus, in solid form, to be absorbed slowly, was suggested by the high mortality rate among these rats, although detailed study of the toxicology was not undertaken here.

2. The immediate hemostatic effect of alginic acid preparations was contrasted with controls of oxidized gauze in the spleen and liver of dogs. There was a marked difference in this property, control of hemorrhage being often difficult to obtain with alginate when oxidized cellulose was immediately effective. Study of these organs at autopsy showed in general, more inflammatory and fibrous tissue response to the alginates than to oxidized cellulose. If anything, the absorption time of the former was longer, but this was not checked in detail. The toxic effects at presumably lower dose levels than those employed by Chenoweth in cats suggests the possibility that the dog is more susceptible to the toxic effects of the alginates than the cat.

3. It was concluded that the advantage of sterilization by autoclave was outweighed by the less effective hemostatic action and by the toxic properties of the alginates, and that further experimental study was not warranted. It was not thought safe to propose these new preparations for trial in clinical surgery.

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THE TOXICITY OF SODIUM ALGINATE IN CATS*

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AN ABSORBABLE, hemostatic and readily manufactured surgical gauze which can be sterilized by autoclaving can be prepared from alginic acid, the product of certain seaweeds. A report on the nature and experimental surgical use of such gauze has been made recently by Blaine[1], who found it to be readily absorbed and concluded that it was a useful hemostatic agent of wide applicability. A report by Solandt[2] indicates that the sodium salt of alginic acid possesses considerable toxicity for rabbits.

Because of the usefulness of absorbable surgical gauzes, the discovery of a material which, on manufacturing grounds, is as suitable as alginic acid, is very important. However, in view of the toxic effects reported by Solandt it appeared necessary to carry out a more extensive examination of the pharmacology of alginates. The present study is an examination of the effects of the administration of alginic acid and some of its derivatives. These are listed and described in Table I.

A. THE TOXICITY OF COMMERCIAL SODIUM ALGINATE (41-125)

This material was obtained as a powder which was soluble in physiologic saline to the extent of one per cent, forming a viscous solution. Three cats were injected intraperitoneally with 250 mg./kg. and two with 100 mg./kg. Larger doses could not be given because of the volume required. These animals were followed for 10 days and then sacrificed with ether (see Table II). In general, the toxic effects produced were not related to the dose of alginate administered. Only one animal, one which received 250 mg./kg., was moribund at the time of sacrifice. This animal failed to eat after the injection and became progressively more depressed. During this 10 day period the animal manifested proteinuria and hematuria. Although on examination of the abdomen it appeared that most of the injected alginate was still present, on microscopic examination the kidney tubules were found to be completely occluded by erythrocytes, indicating considerable absorption and toxicity.

The other animals of this series vomited frequently on the day of injection and were depressed and disinterested in food on the following day. All animals showed definite depression of cortical reflexes (placing)* and some ataxia. In two cases recovery occurred in about five days while in the remaining three animals the abnormalities persisted until sacrifice.

Urine secretion was suppressed in all animals for one to three days, followed by the secretion of small amounts of urine containing considerable protein. Both volume and protein content had returned to normal three or four days after the injection.

* *Placing Reactions:* A group of cortical reflexes concerned with proprioceptive maintenance of posture.

** The expenses of this investigation were defrayed by a grant from Johnson and Johnson.

On examination of the sacrificed cats it was found that absorption had been very irregular, probably accounting for the absence of a relation between the dose injected and the effects produced. The peritoneum, however, showed no signs of irritation. Apart from a small hemorrhagic area in one lung, found microscopically to be associated with a vein occluded by hyaline, palely basophilic material (alginic acid?), no gross damages were noted. Microscopic examination of the kidneys revealed extravasation of the blood into the tubules, varying in degree from slight to extreme. The tubular epithelium

TABLE I.—*Characteristics of Substances Examined**

Sample Number	Chemical Nature	Supplied as	Partial Analysis per cent‡ COOH	Ca	K	N	CH_2O	Nitration
41-116	Alginic acid	Gauze‡	22.1	0.10	2.5	..	None	None
41-125	Sodium alginate	Powder	..	0.0	0.0	..	None	None
41-151	Di-aldehyde alginic acid	Gauze	22.1	0.0	0.0	0.2	0.11	None
41-152	Di-aldehyde alginic acid (contains 2% octyl pyridium bromide, a sizing agent.)	Gauze	22.1	0.0	0.0	0.3	0.11	None
89-31†	Decarboxylated, nitrated alginic acid	Gauze	16.3	0.0	..	4.0	Trace	38
89-32†	Decarboxylated, nitrated alginic acid	Gauze	14.6	0.0	..	4.7	Trace	45

*Aqueous solutions are negative to the usual tests for protein and reducing substances.
**Analyses supplied by the manufacturer.
†Reduce Benedict's solution.
‡Woven in a tubular form known as stockinette

TABLE II.—*Toxicity of Commercial Sodium Alginate Solution Following Intraperitoneal Injection (41-125)*
(By Single Injection)

Experiment Number	Dose mgm./kg.	Died (D) or Sacrificed (S)	Duration of Experiment	Degree of Effect	Comment
15	250	S	11 days	4+	Moribund
17	250	S	9 days	1+	
18	250	S	9 days	1+	
16	100	S	11 days	2+	
19	100	S	11 days	1-2+	

The presence of one or more of the following conditions was used to establish the "degree of effect".
1+ = slight ataxia, depressed, placing reflexes slightly depressed.
2+ = ataxia, placing reflexes depressed, moderate proteinuria.
3+ = prostrate, extreme proteinuria, smaller intracardiac clots.
4+ = Dead or moribund, anuric, larger intracardiac clots.

appeared to be slightly damaged but assurance on this point is not possible because of the distorting effect of the fat content of the normal cat tubules. The liver lobules showed some necrosis, particularly of the central type, while in two animals which had received doses of 250 mg./kg. there were areas in which the nuclei were darkly stained and pyknotic and the cytoplasm of large areas had a fused, amorphous appearance and, although still acidophilic, were much more intensely stained.

B. THE TOXICITY OF ALGINATE GAUZE (41-116).*

This sample was a gauze, which consisted of the partial calcium salt of alginic acid suitably prepared for surgical use. A five per cent solution was prepared by dissolving the gauze in sodium bicarbonte. The solution, although somewhat viscous, was easily injected intravenously and intraperitoneally in cats. The results of these experiments are presented in Tables III and IV. It is apparent that the preparation was decidedly toxic.

The animals, following injection by either route, rapidly became depressed, vomited frequently and showed no interest in food on the day of the injection.

TABLE III.—*Toxicity of Alginic Acid (41-116) Solution Following Intraperitoneal Injection (By single injection)*

Experiment Number	Dose mg./kg.	Died (D) or Sacrificed (S)	Duration of Experiment	Degree of Effect	Comment
9	500	D	1 day	4+	Antemortem clot
10	250	D	1 day	4+	" "
14	250	D	1 day	4+	" "
12	100	S	7 days	3-4+	" "
13	100	S	7 days	1+	
8	25	S	10+ days	1+	
11	25	S	10+ days	1+	

TABLE IV.—*Toxicity of Alginic Acid (41-116) Solution Following Intravenous Injection (By Single Injection)*

Experiment Number	Dose mg./kg.	Died (D) or Sacrificed (S)	Duration of Experiment	Degree of Effect	Comment
2	500	D	5 Days	4+	
3	500	D	1 day	4+	
4	500	D	2 days	4+	
6	500	D	4 days	4+	Antemortem clots
5	316	D	1 day	4+	" "
1	250	D	2 days	4+	Anuric
7	250	D	2 days	4+	Antemortem clots

The following day many of the animals were moribund, while all except those receiving the smallest doses were markedly depressed. Central nervous system function was obviously impaired, for ataxia was extreme in those animals which could walk at all; placing and righting reflexes were depressed or absent and the animal's reactions to noxious stimuli were feeble.

Animals which did not die during the 24-hour period after injection usually secreted little or no urine during that time, despite the large volume of fluid (10-30 cc.) in which the alginate was administered. When urination recommenced only small amounts of concentrated material were obtained and all contained large amounts of protein, but no reducing substances.

* Same sample as 41-116 used by Frantz 4.

Examination of the animals which died spontaneously or were sacrificed following intraperitoneal injection revealed that practically complete absorption of the alginate occurred if the animals survived more than two days. The peritoneum showed no evidence of irritation and was smooth and glistening when absorption was complete. Occasionally small gelatinous flecks of the unabsorbed material could be detected.

Following both intravenous and intraperitoneal administration the abdominal viscera usually appeared normal by gross inspection although occasionally small hemorrhagic areas could be discerned in the bladder wall and kidney cortex. The lungs were occasionally affected, being hemorrhagic to the point of hepatization in four of the animals receiving the larger doses. Upon opening the chambers of the heart massive pale yellow (antemortem or "chicken fat") clots were visible in nearly half of the animals of these groups. The clots were firmly attached to the wall of the chamber and frequently extended through the valves, coalescing with clots in the adjacent chambers. In animals which died later in the course of poisoning some organization of these clots was apparent on microscopic examination. In one animal in which no clots could be found, there were extensive subendocardial hemorrhages in the left ventricular wall. No significant difference in the incidence of these changes between the intravenously and intraperitoneally injected groups could be detected.

Microscopic examination revealed varying degrees of renal tubular damage. In the most severe cases the epithelium of the tubules of the loop of Henle was completely separated from the basement membrane, the nuclei were pyknotic and darkly stained and most of the papillary ducts were occluded with basophilic casts (alginic acid?) containing cell fragments.

The liver frequently contained areas in which the entire cytoarchitecture was disrupted by necrosis and fragmentation of the cells. Other areas were evenly acidophilic and no cell structure could be discerned. No increase of basophilic material which might be interpreted as storage of alginate was found.

Examination of the brain, lungs and adrenals occasionally revealed a thrombosed blood vessel containing hyaline, basophilic material. In the cerebellum degeneration of neurones was noted in discrete areas, suggesting occlusion of the blood supply to such areas.

C. TOXICITY OF DI-ALDEHYDE ALGINIC ACID GAUZE (41-151, 152)*

It was reasoned (see also Solandt) that the coagulation noted with alginate was the result of its ability to form firm gels with calcium salts. Oxidizing alginic acid with periodic acid produces a di-aldehyde structure by cleavage of the ring at the 2-3 carbon linkage, resulting in a substance which is actively hemostatic and at the same time does not form a strong gel with calcium salts.

* These compounds were prepared by Dr. James J. Eberl for the purposes of this investigation.

Although gauze prepared from this material required formaldehyde sterilization it appeared feasible to employ it in surgery.

As shown in Table V cats were injected intraperitoneally with various doses of this material (41-151) in a 2.6 per cent solution of the sodium salt. These animals followed a course similar to the animals described above. One animal died, although it had received the smallest dose, however, it was in the early stages of pregnancy. The pattern of the course of poisoning in this animal was typical of alginate intoxication, although grossly the post-mortem examination was negative. Only one of the remaining animals failed to show ataxia or depression of the placing reflex. In four, the placing reflexes were

TABLE V.—*Toxicity of Di-Aldehyde Alginic Acid (Following Single Intraperitoneal Injection)*

Experiment Number	Dose mg./kg.	Died (D) or Sacrificed (S)	Duration of Experiment	Degree of Effect	Comment
41-151					
26	500	S	8 days	2+	
27	500	S	10 days	1+	
37	500	S	8 days	3+	Antemortem clots
38	500	S	9 days	4+	" "
39	500	S	9 days	1+	" "
40	500	S	9 days	3+	" "
41	500	S	9 days	3+	
29	250	S	8 days	1-2+	
28	250	S	8 days	3+	
30	125	S	7 days	3+	Falls on walking
31	125	D	5 days	4+	" " " Pregnant
41-152					
25	125	S	12 days	0-1+	
24	125	S	7	0	
22	250	S	9	1+	
23	250	S	9	0	
20	500	S	10	0-1+	Did not eat
21	500	D	4	4+	Occasional convulsions

absent and ataxia was so severe as to render locomotion nearly impossible, the degree of impairment being apparently independent of the dose. All were depressed, inactive and unaggressive. In these cats the evidence of central nervous system damage persisted until sacrifice, while the other less affected cats recovered rapidly. Some degree of kidney damage was frequent as indicated by the occurrence of proteinuria and hematuria. Urine secretion was suppressed or very slight on the first day after the injection but diuresis subsequently occurred and persisted for a day or two.

Post-mortem examination of the sacrificed animals revealed that practically complete absorption of the solution had occurred, leaving the peritoneum without evidence of irritation. The hearts of five of the cats receiving 500 mg./kg. doses contained typical ante-mortem clots varying in size from one millimeter in both dimensions to massive clots several centimeters long and

nearly a centimeter in diameter. Although intracardiac clotting had been anticipated following its occurrence with alginic acid, no signs or symptoms indicative of the phenomenon could be detected prior to death.

Five test animals and one uninjected control were studied for one week before and one week after the intraperitoneal injection of 500 mg./kg. of di-aldehyde alginic acid (Table V and Table VI). In view of the observation

TABLE VI.—*Results of Laboratory Tests on Cats Receiving Single Intraperitoneal Doses of 500 mg.-kg. of Di-Aldehyde Alginic Acid*

Experiment Number	Days	NPN mg%	Sedimentation rate mm./hr.	Per Cent RBC	Urine
36	0	47	17.0	38	Negative
	9	47	7.0	40	Negative
37	0	55	0.7	..	..
	7	63	1.0	50	Negative
	Injected				
	11	47.4	17.0	48	4 + protein
	16	45	11.0	41	3 + protein
38	0	41	26.9	..	Negative
	7	47	..	..	..
	Injected				
	11	55	63.0	28	3 + protein
	16	44	55.0	30	2 + protein
39	0	45	16.7	..	..
	8	63	8.0	41	..
	Injected				
	11	42	53.0	37	3 + protein
	16	47	30.0	39	Negative
40	0	47	7.8	..	Negative
	7	50	1.0	42	..
	Injected				
	11	41	57.0	27	Negative
	16	48	56.0	31	Negative
41	0	52	7.8	..	..
	8	51	0.2	42	..
	Injected				
	11	59	24.0	48	3 + protein
	16	66	22.0	40	Negative

of Solandt[2] that sodium alginate increased the sedimentation rate of erythrocytes the erythrocyte sedimentation rate was determined as well as the per cent erythrocytes. Urine was examined for protein and reducing substances and blood non-protein nitrogen levels were determined. The occurrence of protein in the urine and a marked increase in the sedimentation rate following the injection were the only changes of significance noted. The blood non-protein nitrogen levels were variable, as is so often the case in cats, but were not significantly changed.

Six animals were studied in a similar fashion except that the gauze was shredded and introduced through a small incision into the peritoneal cavity. Doses of 100, 250, and 500 mg./kg. were given in this fashion. Although

some depression and occasional vomiting occurred for several days after the operation, there was little evidence of significant central nervous system involvement. Proteinuria and an increased sedimentation rate were observed in all but one animal (100 mg./kg.) and persisted for five to ten days. On post-mortem examination the gauze was found to have been well absorbed although the peritoneal cavity usually contained ten to twenty cubic centimeters of pinkish watery fluid, a larger amount than that noted following injection of the dissolved material. No other pathologic changes were observed with the exception of one small ante-mortem clot in the left ventricle of a cat receiving a dose of 250 mg./kg.

A sample (41-152) of similar material was obtained which contained approximately 2 per cent of "Fixanol" (octyl pyridinium bromide), a sizing

TABLE VII.—*Toxicity of Decarboxylated, Nitrated Alginate Gauzes (89-31, 32) (By Single Injection)*

Experiment Number	Dose Mg./kg.	Route	Sacrificed (S)	Duration of Experiment	Degree of Effect	Comment
89-31						
50	500	I.P	S	4 days	4+	Multiple massive hemorrhages
55	500	I.V.	D	1 day	4+	
51	250	I.P.	D	1 day	4+	
56	250	I.P.	S	5 days	1+	
57	250	I.P.	D	5 days	4+	
52	100	I.P.	—	—	0+	Polyuria
89-32						
65	500	I.P.	D	3 days	4+	Massive hemorrhage
67	500	I.P.	D	1 day	4+	
66	250	I.P.	S	5 days	4+	

agent used to prevent the monofilaments of alginic acid from sticking together. In view of the unsatisfactory nature of the unsized preparation (41-151) the sized preparation was examined less thoroughly. One death at a high dose level and three animals typically affected to a lesser degree, were obtained in a series of six cats (Table V). It is improbable that thread sizing decreases the toxicity of alginic acid and it evidently does not increase it.

It is apparent that the reduced gelling capabilities of the di-aldehye alginate preparation were still sufficient to cause serious vascular occlusion. The modified gauze was readily absorbed but too toxic to be clinically useful.

D. THE TOXICITY OF NITRATED SODIUM ALGINATE (89-31, 32)

Cats were injected intraperitoneally with a sodium bicarbonate solution of an alginate gauze prepared by decarboxylating and nitrating alginic acid (see Table I). These experiments are listed in Table VII.

This material was markedly toxic. Vomiting, depression and ataxia were present as previously described, but in addition there developed a hemorrhagic diathisis manifested by bleeding and swollen gums, hemorrhages and hematuria. On post-mortem examination extensive hemorrhages were found in nearly every organ and the blood did not clot within an hour after withdrawal.

Urine from these animals reduced Benedict's solution, differing in this respect from the other alginates studied but resembling oxidized oxycellulose (q.v.). It is apparent that nitration and decarboxylation of alginate do not produce a usable gauze.

E. COMPARATIVE EXAMINATION OF OXIDIZED CELLULOSE GAUZE

A series of ten cats was studied in which intraperitoneal injections were made of a sodium bicarbonate solution of a sample of oxidized cellulose gauze. Following the injection no vomiting occurred. No abnormalities of behavior were noted on subsequent days with the exception of the two animals (67, 70) described in Table VIII. These had depressed or readily fatigued placing reflexes for a few days, which returned to normal in about a week. All cats

TABLE VIII.—*Toxicity of Oxidized Cellulose Gauze Following Intraperitoneal Injection of a Sodium Bicarbonate Solution of the Gauze (By Single Injection)*

Experiment Number	Dose Mg./kg.	Died (D) or Sacrificed (S)	Duration of Experiment	Degree of Effect	Comment
32	500	S	7 days	0	
34	500	S	6 days	0	
65	500	S	14 days	0	
67	500	S	14 days	0-1	Placing reflexes depressed for 5 days
68	500	S	14 days	0	
33	250	S	13 days	0	
35	250	S	5 days	0	
66	250	S	14 days	0-1	Placing reflexes easily fatigued
69	250	S	14 days	0	
70	250	S	14 days	0	

developed proteinuria one or two days after the injection. Within five days this had ceased but during the entire period of the experiment after the administration of oxidized cellulose their urine reduced Benedict's solution. Oxidized cellulose itself readily reduces Benedict's solution so that it may be presumed that oxy-cellulose, or portions of its molecule, were excreted in the urine.

No animals died nor were any noticeably affected by their experience. When sacrificed, post-mortem examination revealed that absorption was complete. No gross pathologic changes were noted and there was no evidence of intravascular clotting. It is apparent that oxidized cellulose is much less than alginic acid.

DISCUSSION

As the result of this study of the action of alginic gauzes in the animal body the material can not be recommended for surgical use as an absorbable gauze. It would seem that the ability of alginic acid to form gels with calcium,[1, 2] which may or may not be the mechanism underlying its hemostatic action, is sufficient to cause serious localized circulatory embarrassment.

Apart from this action, the production of hepatic and renal impairment is a contraindication for its use.

The present study largely made use of parenteral injection of solutions of the various alignates and it may be argued that the production of toxic reactions by such means does not form an appropriate basis for clinical evaluation, none the less, intravenous administration of even larger doses of oxidized cellulose has been shown to be innocuous.[3] This was completely confirmed in the small series of cats presented in the present report.

While the experiments in which the shredded, relatively innocuous di-aldehyde alginic acid was introduced into the peritoneal cavity were not attended by evidence of marked toxicity its use has not been very satisfactory in experimental surgery.[4] Although Blaine[1] did not report any toxic effects from the use of alginate materials the present studies indicate that it is not without danger for clinical use.

Solandt's[2] observation that alginic acid increases the sedimentation rate was confirmed. It was noted during *in vitro* studies of this phenomenon that the hemoglobin of cells caused to settle in this fashion was not readily oxygenated on agitation. This has also been reported for acacia.[5] Although efforts were made to demonstrate a lowered arterial or venous oxygen content such as was reported for acacia no definite conclusions could be drawn from the data. It may be inferred that this action of alginic acid is not of major importance as a cause of its toxicity.

SUMMARY

1. The intraperitoneal or intravenous injection in cats of solutions of sodium alignate results in the production of large ante-mortem intracardiac clots.
2. Evidence is presented that injury to the brain, liver and kidney frequently occurs. Alginic acid shares with other gums the ability to accelerate the sedimentation of erythrocytes.
3. A di-aldehyde derivative of alginic acid is slightly less toxic than alginic acid while a nitrated derivative is more toxic and in addition greatly prolongs clotting time *in vivo*.

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SIGNIFICANT ANATOMIC RELATIONS IN THE SYNDROME OF THE SCALENE MUSCLES

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THE GROUP OF SYMPTOMS commonly referred to as the scalenus anticus syndrome seems more likely to develop in certain persons than in others. Bilateral dissections of the area in question were done on 56 cadavers in an effort to discover significant anatomic relations to explain this fact. Particular attention was directed toward the modifications in structure and anatomic relations of the scalene muscles, the components of the brachial plexus and the adjacent vessels.

It should be recalled that originally this set of symptoms was associated only with the presence of a cervical rib and was designated as the syndrome of the cervical rib. Subsequent investigations further clarified the problem and demonstrated that other factors entered into the production of the syndrome. The syndrome of the cervical rib was described by Murphy[1] as including any or all the following: 1) pressure on the trunks of the brachial plexus with pain, paresthesia, hypesthesia, or anesthesia in the peripheral area of distribution of the involved sensory fibers, and paresis or paralysis of the muscles supplied by the involved motor fibers, 2) pressure on the subclavian artery with brachial ischemia and possible aneurysmal formation, thrombosis and gangrene, and 3) development of a tumor in the supraclavicular triangle. The fact that this syndrome might occur in the absence of a bony anomaly was recognized by Murphy,[2] who described a case which presented many of the manifestations of the cervical rib syndrome but no cervical rib was present. At operation the lower trunk of the brachial plexus was found on the inferior portion of the anterolateral border of the scalenus medius muscle. The insertion of the muscle at that point was severed and the subjacent portion of the rib resected. There was complete relief of symptoms. Jones[3] stated that in some individuals the eighth cervical and first thoracic segments contribute an unusually large proportion of the fibers to the brachial plexus and in these cases the first thoracic rib may traumatize the lower trunk of the plexus. Post-fixation of the brachial plexus was the term applied to those cases in which a comparatively large number of the component fibers emerge through the lower contributing segments. A plexus which received a relatively large number of fibers from the upper contributing segments was termed pre-fixed. Wilson[4] described two main types of muscular involvement by cervical ribs. One was designated the median type because some or all the

intrinsic muscules of the hand supplied by the median nerves were involved. These patients usually also demonstrated sensory impairment of the lateral portion of the forearm and hand. The other type, stated to be the more common, included those cases exhibiting involvement of the intrinsic hand muscles supplies by the ulnar nerve. Atrophy or weakness of these muscles usually was accompanied by sensory phenomena in the peripheral area supplied by the ulnar nerve. Wilson noted that in several patients hypesthesia or anesthesia was confined to the peripheral area usually assigned to the sixth cervical nerve. He stated that this root is not involved by a cervical rib but attempted to explain the observation by stating that these might also represent cases of post-fixation of the brachial plexus in which the seventh cervical nerve and not the sixth was involved.

Much of the clarification of the cervical rib and scalene syndromes is the result of Todd's work.[5-9] He accounted for the reportedly higher incidence of these symptoms in females on the basis of muscular development and respiratory activity. He believed that because of the relatively poor development of the trapezius muscle in females, the shoulder would assume a comparatively lower position in relation to the thorax than in males. He also stated that the comparatively poor development of the rectus abdominis muscles of females might allow the skeletal structure of the thorax to adopt a relatively higher position than in males. Todd suggested further that the symptoms might occur more frequently in women because of their greater use of the upper thoracic muscles in respiration. He disagreed with previous statements that the subclavian artery could be compressed by the scalenus anticus muscle or the first rib. He believed that the vascular symptoms in cases of cervical rib syndrome are not mechanical in origin but trophic in character and are caused by involvement of the sympathetic fibers passing across the first rib to enter the lower trunk of the brachial plexus.

The theories of both Jones and Todd were supported by Stopford,[10] who stressed the importance of the first thoracic rib as an etiologic factor in neuritis of the lower trunk of the brachial plexus. He believed, as did Jones, that a predisposing factor is the anatomic relation of the nerve trunk and the rib, when the bone is bevelled by a trunk which received a large contribution from the upper two thoracic roots. He also agreed with Todd that the anatomic changes of the shoulder in relation to the trunk are important factors in the onset of symptoms. It was reiterated that the medial portion of the clavicle may be elevated or depressed depending upon the tonicity and development of the rectus abdominis muscles and that the position of the lateral portion may be similarly changed depending upon the strength and tone of the trapezius muscle. He concluded that these two factors acting on the clavicle are of importance in the production of compression of the lower trunk of the brachial plexus by the first rib and also explain the greater incidence of this syndrome in females.

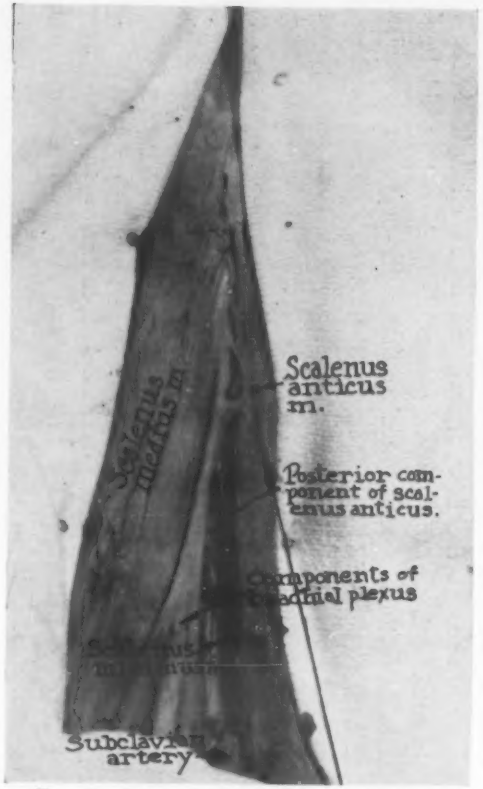

FIG. 1.—Lateral view of supraclavicular area showing relations of "posterior component" of the scalenus anticus, main body of scalenus anticus, scalenus minimus and medis, brachial plexus and subclavian artery.

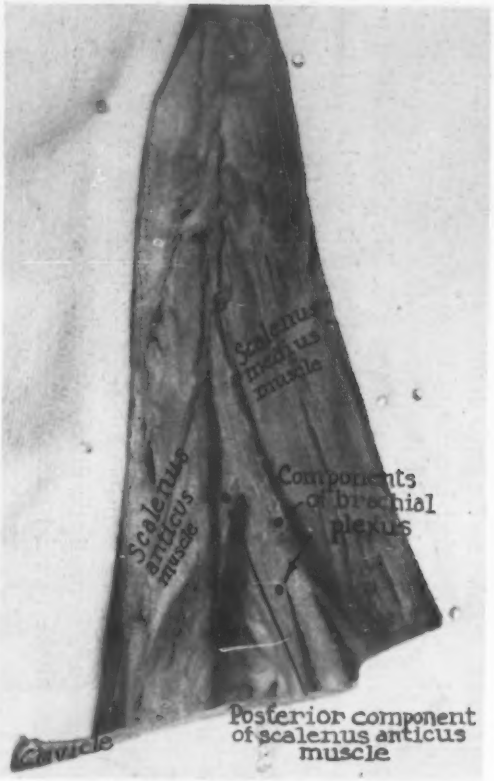
Scalenus medius muscle
Scalenus anticus muscle
Components of brachial plexus
Posterior component of scalenus anticus muscle

FIG. 2.—Anterolateral view of supraclavicular area showing relations of "posterior component" of the scalenus anticus t othe remainder of the muscle and to the brachial plexus.

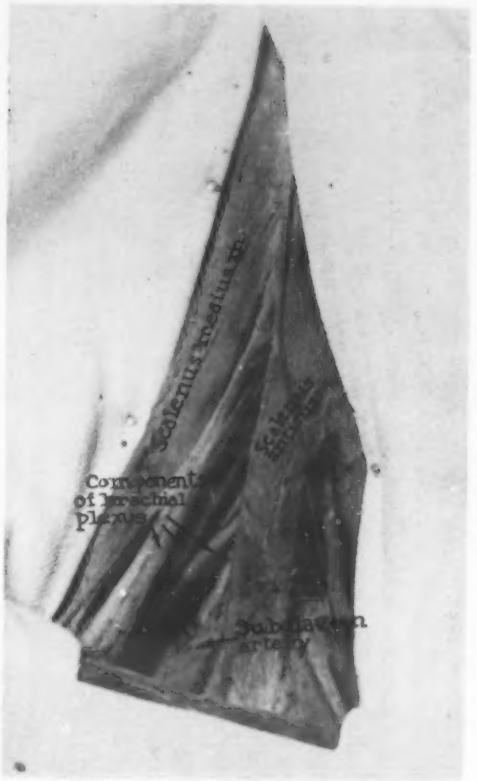

FIG. 3—Anterolateral view of supraclavicular area showing relations of brachial plexus, subclavian artery and the scalenus anticus and medius muscles.

Brickner and Milch[11] similarly reemphasized the significance of the relation of the position of the shoulder to the thorax in the production of the symptoms characteristic of the cervical rib syndrome either in the presence of a cervical rib or with a normal first thoracic rib.

Adson and Coffey[12] disagreed with Todd's statement that the contracting scalenus anticus muscle could not compress the subclavian artery. They reported having demonstrated such an action by this muscle by having the patient elevate the chin and extend the neck or rotate the head to the affected side while making a deep inspiration. This resulted in obliteration of the pulse at the wrist on the affected side as well as production of paresthesia in the distribution of the brachial plexus. They advocated that the cervical rib not be removed for the relief of symptoms but that only the scalenus anticus muscle be severed. In their series of cases of cervical ribs 45 per cent exhibited symptoms referable to the anomalous ribs. However, Torelli[13] reported that only nine of 100 patients with cervical ribs whom he had examined presented evidence that the anomalous rib was causing symptoms. He estimated the incidence of cervical ribs in a large series of cases to be about 2 per cent.

Ochsner, Gage and DeBakey[14] agreed that post-fixation of the brachial plexus or poor development of the elevator muscles of the shoulder or the rectus abdominis muscles may constitute predisposing factors for the development of the scalenus anticus syndrome, but they suggested that spasm of the scalenus anticus muscle resulting from irritation of somatic efferent fibers passing to the muscle in the traumatized brachial plexus caused additional elevation of the first rib with further trauma to the brachial plexus and more muscle spasm. Thus, it was postulated a vicious circle was established which must be broken for relief of the discomfort and could be done so most practically by anterior scalenotomy. They stated that the brachial plexus and subclavian artery are pinched between the scalenus anticus and medius muscles during the phase of muscular spasm. Naffziger and Grant[15] in reporting a series of cases of what was termed scalenus syndrome agreed essentially with previous theories of etiology.

Trauma was believed to have been the precipitating factor in 29 of 115 cases of scalenus anticus syndrome reported by Jelsma.[16] Semmes and Murphey[17] discussed the simulation of scalenus anticus syndrome by a herniated sixth clavical intervertebral disk.

Swank and Simeone[18] concluded that the individual portions of the scalenus anticus muscle which arise from the anterior surfaces of the transverse processes of the third, fourth, fifth, and sixth cervical vertebrae can compress the subjacent cervical nerve root as it passes laterally and inferiorly to join the brachial plexus. Primarily on these grounds they explained the various combinations of symptoms which may be seen with spastic scalene muscles.

It should be borne in mind that it has been adequately demonstrated that the same complex of symptoms indicative of trauma to the brachial plexus

FIG 4.—Anterolateral view of supraclavicular area showing ferior curved portion of anterolateral border of scalenus medius and its approximation to the scalenus anticus.

may be found in the presence of a cervical rib or without an osseous anomaly. In the former case the term, *cervical rib syndrome,* may be used and in the latter the term, *scalenus anticus syndrome,* has been applied. Even though the cervical rib is small, it may be the key to the solution of the patient's difficulty, for sometimes a firm, fibrous cord extends from the tip of the cervical rib to be attached to the first thoracic rib and thus serves as a ridge

across which the lower trunk of the brachial plexus may be traumatized. However, the anatomic data which we will present indicates that the terms "the syndrome of the scalene muscles" or "the scalene syndrome" are more suitable when there is no roentgenologic evidence of pathologic change. It is evident from this investigation that some term should be used which does not

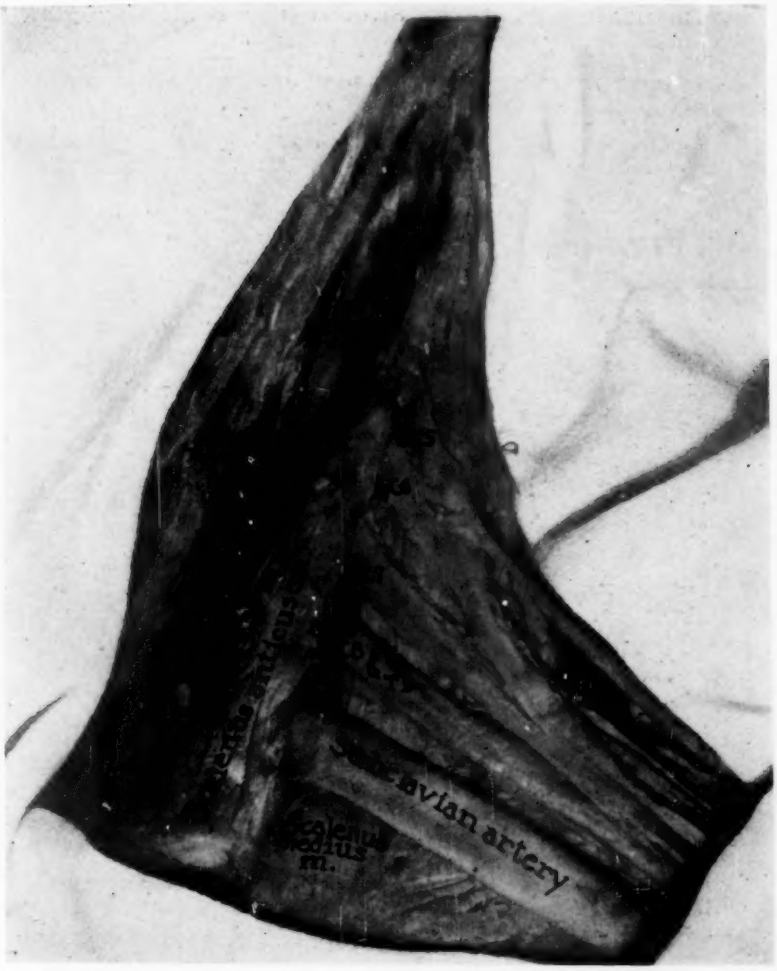

FIG. 5.—Anterolateral view of supraclavicular area showing close approximation of scalenus medius and anticus and angulation of the lower components of brachial plexs and subclavian artery across anterolateral border of scalenus medius.

confine the implication of a pathologic change to the scalenus anticus muscle.

It is apparent from a review of the literature that the factors which have been considered of greatest importance in the development of the "scalenus anticus syndrome" include post-fixation of the brachial plexus, an unusually low position of the upper extremity in relation to the thorax, or a relatively

high position of the thorax in relation to the upper extremity, and the state of contraction of the scalenus anticus muscle. Most investigators apparently believe that a combination of all these factors generally is present. The scalenus medius muscle has been given little credit for participating significantly in the production of symptoms. However, Ochsner and associates[14] stated that the brachial plexus may be compressed between the scalenus anticus and medius muscles with increased irritation to the plexus, and Telford

FIG. 6.—Anterolateral view of supraclavicular area showing usual relation of the anterolateral border of the scalenus medius to the anticus, subclavian artery and brachial plexus.

and Mottershead[19] suggested that traction of the brachial plexus across the anterior margin of the scalenus medius muscle may irritate the component nerve fibers. We[20] presented evidence before the American Association of Anatomists in April, 1947, that the anatomic relations and the state of contraction of the scalenus medius muscle may be the major factors in the production of the syndrome usually referred to as the scalenus anticus syndrome.

It is of interest to recall that most patients with this syndrome have no bony anatomic anomaly on which to blame the production of symptoms. Moreover, only approximately 10 per cent of individuals with one or more of

the bony anatomic variants frequently associated with this syndrome ever show any of its manifestations. Furthermore, many patients with a herniated cervical intervertebral disk or other lesion causing nerve root irritation exhibit extreme scalene muscle spasm without evidence of any of the described types of scalenus anticus syndrome. Therefore, one would conclude that the syndrome of the scalene muscles is more likely to develop in certain individuals than others for reasons which are not apparent by roentgenographic examination.

The soft tissue structures which have been considered of possible significance in the production of this syndrome and which have been examined in

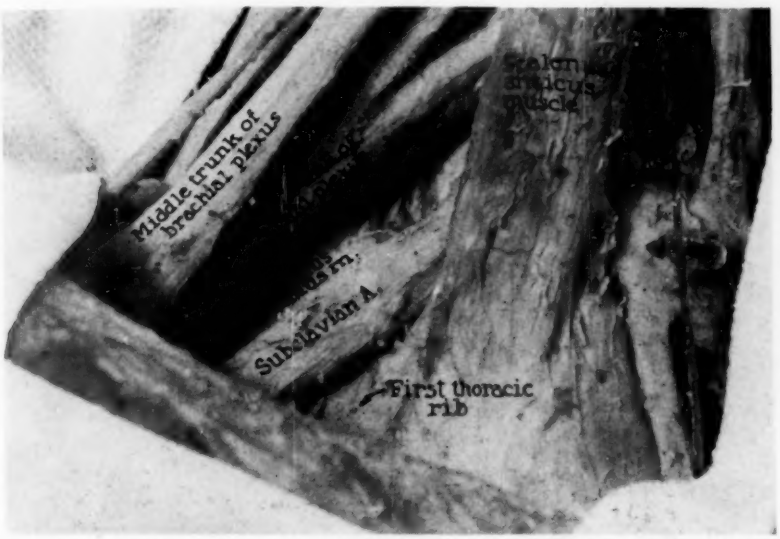

FIG. 7.—Anterior view of supraclavicular area showing usual relations of scalenus medius and anticus at their insertions.

detail in this group of dissections include the following:

1. *Scalenus anticus muscle.* In all cases, most of the fibers of this muscle arose from the anterior or inferior surface of the anterior tubercles of the cervical transverse processes from the third to the sixth cervical vertebrae inclusive. These fibers, even if in marked spasm, are not strategically located to compress adjacent roots of the brachial plexus (Figs. 1, 2, 3, 9a and 10b). The only possible way for this portion of the muscle to contribute to the syndrome is by elevation of the rib to which it is inserted with consequent trauma to the lower trunk of the brachial plexus. It is possible that such elevation of the first thoracic rib might, in some cases, constrict the lumen of the subclavian artery. The artery may also be compressed by being displaced forward by the scalenus medius against a spastically contracted scalenus anticus muscle (Figs. 5 and 10a). However, in most cases muscle fibers arose from the inferior margin of the groove of the transverse process in which each nerve root lay, as well as from the posterior tubercle of the transverse

process (Figs. 1, 2, 6, 9b, 11, 12a and b, and 13a and b) and passed inferiorly and anteriorly to join the body of the scalenus anticus muscle and insert with the fibers arising from the anterior surface of the transverse processes. Those fibers having an attachment of origin from the posterior tubercle of the transverse processes have an origin in common with the fibers of the scalenus medius muscle (Figs. 1 and 2). These might be termed the "posterior" components of the scalenus anticus muscle. Similar bundles of muscle fibers

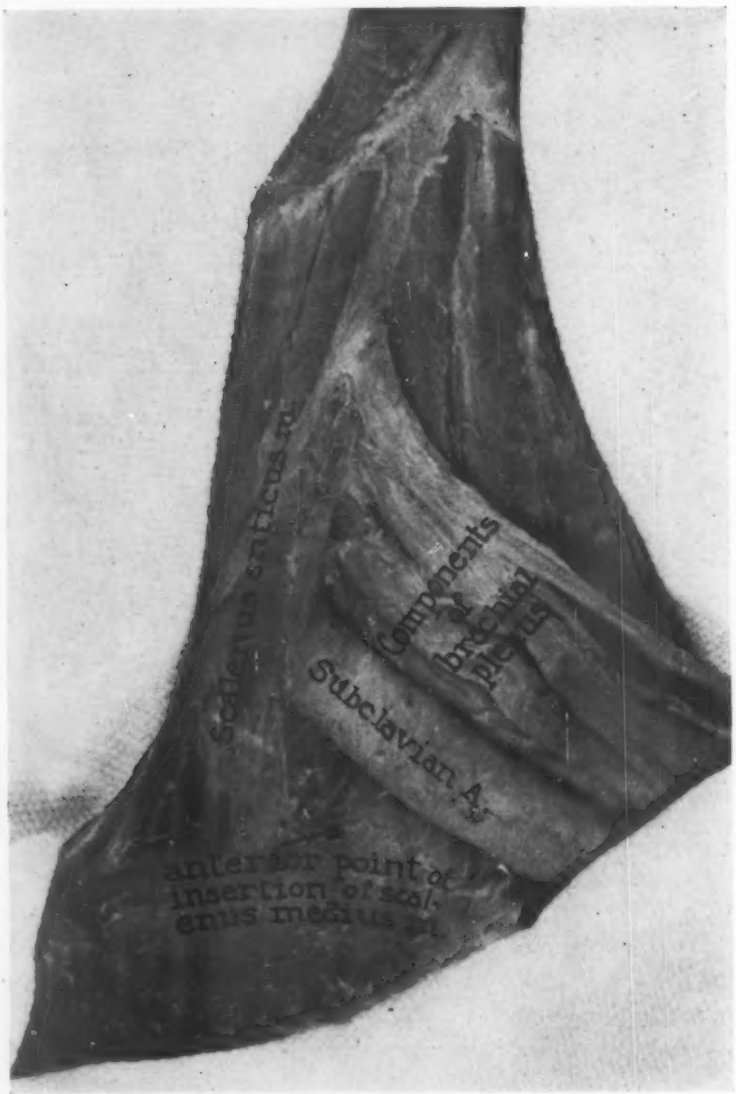

FIG. 8.—Anterolateral view of supraclavicular area showing close approximation of scalenus anticus and medius at their insertions with angulation of subclavian artery and components of brachial plexus across anterolateral border of scalenus medius.

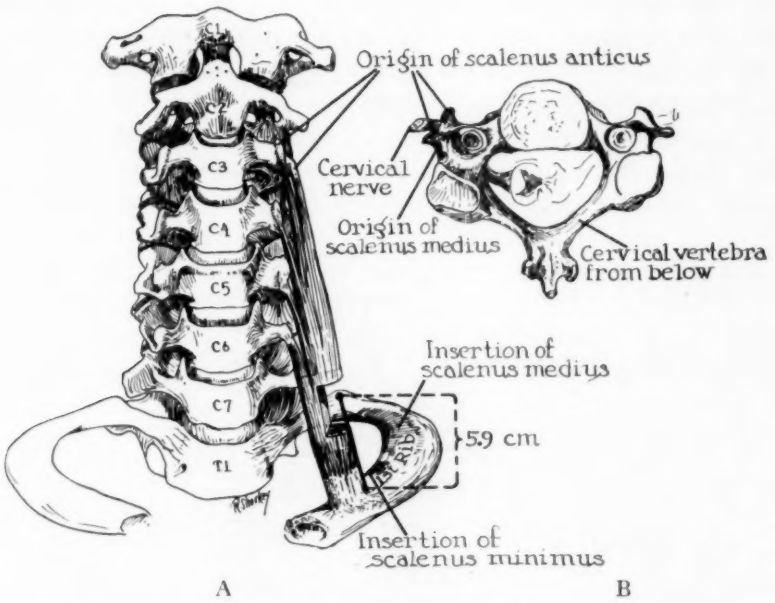

FIG. 9.—(A) Anterior view of scalenus anticus and related bony structures. Average distance of insertion of scalenus anticus from the tubercle of the rib is indicated as determined on the left in 43 male bodies. (B) Inferior view of cervical vertebra indicating areas of origin of scalenus anticus and medius.

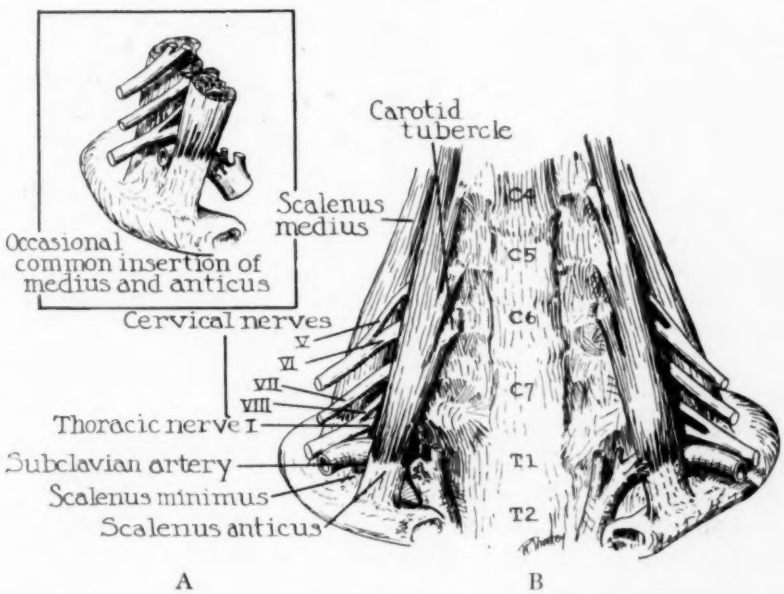

FIG. 10.—(A) Diagram showing close approximation of scalenus anticus and medius at their insertion. (B) Anterior view of lower cervical and upper thoracic regions showing relations of scalenus anticus, minimus and medius, brachial plexus and subclavian artery.

may have their origins on the tendons which give rise to the scalenus medius muscle. Such bundles of muscle fibers are situated so that upon contracting they might pinch the root of the brachial plexus emerging immediately below them. These groups of muscle fibers are not to be considered anomalous as they were present in most of the bodies studied. However, their size varied considerably as did their relations with the adjacent nerves and the subclavian artery. In the majority of cases the size of these bundles was so small that

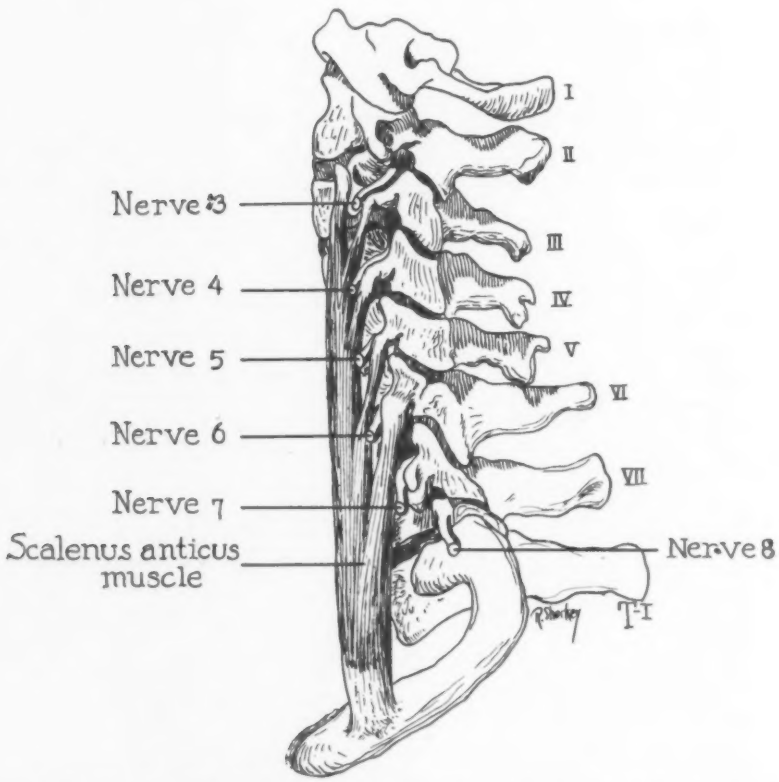

FIG. 11.—Lateral view of scalenus anticus showing relations of its "posterior components" to the main body of the muscle, to the transverse processes and to the nerves.

it was questionable that they would be able to compress the subjacent nerve sufficiently to cause significant irritation of the nerve. The seventh cervical was the nerve most often situated in relation to such a bundle of muscle fibers of apparently significant size (Fig. 11). In some instances, muscle fibers arose posterior and inferior to the sixth cervical component to the brachial plexus, passed in front of the seventh cervical component, then posteriorily to descend behind the subclavian artery, and finally anteriorly to insert with the scalenus anticus muscle (Fig. 13b). In other cases, muscle fibers with a similar relationship to the seventh cervical nerve inserted with the scalenus minimus or

medius (Figs. 12a and b). It is obvious that bundles of muscle fibers which have such a relationship to the seventh cervical nerve, the subclavian artery, and the lower trunk of the brachial plexus might exert undue pressure on these structures. Similar components of the scalenus anticus were commonly present in relation to the fifth and sixth cervical nerves.

A factor in the effectiveness with which the scalenus anticus elevates the first rib is the distance between the insertion of the muscle on the rib and the articulation of the tubercle of the rib. The greater this distance, the more efficiently the muscle can elevate the rib. In 43 male bodies examined this distance averaged 6.0 cm. on the right and 5.9 cm. on the left (Fig. 9a). The measurement ranged from 6.4 cm. to 5.2 cm. on the right and from 6.8 cm. to 4.9 cm. on the left. In 13 female bodies examined this distance averaged

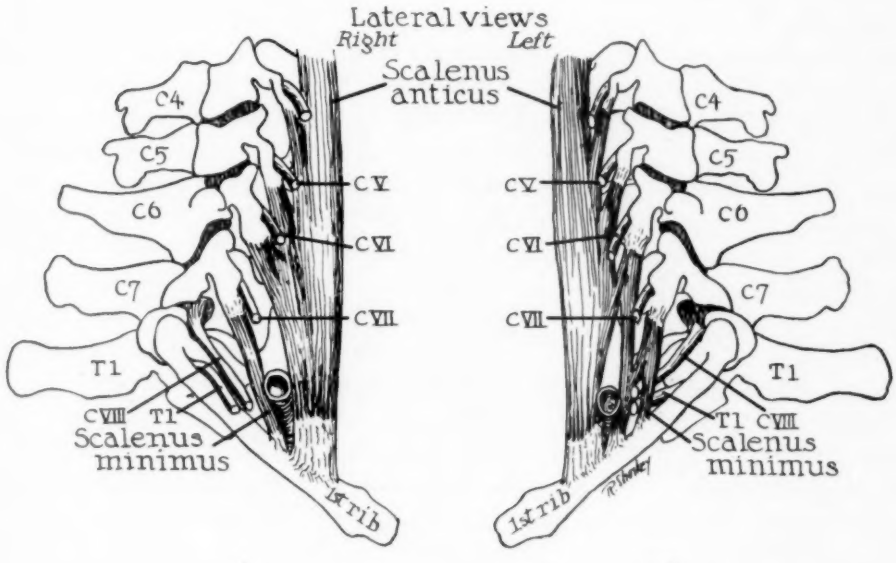

FIG. 12—(A and B.) Lateral view of scalenus anticus and minimus showing unusual relations to lower components of brachial plexus and to the subclavian artery.

5.8 cm. on the right and 6.0 cm. on the left. On the right the distance ranged from 6.6 cm. to 5.0 cm. and on the left from 6.6 cm. to 5.3 cm.

The shorter this distance, the more intimately the muscle is related to the subclavian artery. However, in no instance was it apparent that the bulk of the muscle, that is, the portion arising from the anterior tubercles of the cervical transverse processes, was situated so that it might, by itself, compress the subclavian artery regardless of the degree of spasm. On the other hand, it seems reasonable to believe that the muscle might elevate the first rib sufficiently to compress the artery (Figs. 4, 5, 6, and 7). Even in the cases in which the attachments to the first rib of the scalenus anticus and scalenus medius muscles were approximated it was evident that neither the subclavian

artery nor the trunks of the brachial plexus could be compressed directly by the main body of the scalenus anticus muscle acting alone.

2. *Scalenus minimus muscle.* This muscle was present on the right in 55.4 per cent and on the left in 56.1 per cent of the dissections. In the majority of instances it was found to arise only from the seventh cervical transverse process (Fig. 12a). Occasionally, additional fibers originated from the sixth cervical transverse process (Figs. 13a and b). The muscle extends inferiorly and laterally to insert on the first rib usually at a point posterior and somewhat lateral to the attachment of the scalenus anticus muscle (Figs. 14b and 15b). In some bodies the width of the insertion of the scalenus minimus was equal to the distance between the attachments of the scalenus anticus and medius. Rarely did its insertion overlap those of the scalenus anticus and medius. In practically all cases the muscle passed behind the subclavian artery and anterior to the lower roots of the brachial plexus from an origin on the seventh cervical transverse process behind the emerging seventh cervical nerve. Usually the relationships and the size of the muscle were such that it did not appear capable of contributing significantly to the complex of symptoms. Just as in the case of the main body of the scalenus anticus, the minimus normally upon contracting would contribute to the symptoms only in so far as it might assist in elevating the first rib. Its location and size are not suitable for the muscle to assist greatly in this activity. However, if the muscle is comparatively large and has a wide insertion extending close to or overlapping that of the scalenus medius, it is strategically situated to function as one of the jaws of a vise in which the eighth cervical and first thoracic nerves may be trapped (Figs. 15a and 15b). The opposing jaw of the vise would be the scalenus medius muscle.

Infrequently, the fibers of the scalenus minimus had a complex relation to adjacent structures. For example, fibers sometimes arose from the posterior margin of the sixth cervical transverse process and descended anterior to the seventh cervical nerve, but inserted behind the subclavian artery or even posterior to the eighth cervical and first thoracic nerves (Fig. 12b). Such a relationship would allow the spastically contracted muscle to have a maximum of leverage upon the adjacent nerves and artery.

3. *Vertebrocostal ligament.* This ligament occupied the characteristic position of the scalenus minimus muscle bilaterally in 10.7 per cent and unilaterally in 3.5 per cent of the dissections. The attachments were found to be similar. In an analysis of the activity of this ligament in the production of symptoms of the syndrone of the scalene muscles, it should be pointed out that the ligament becomes relaxed as the rib is elevated. Thus, it might act less effectively than the scalenus minimus muscle as one of the jaws of a vise in which the lower roots of the brachial plexus might be pinched. The situation in which it would carry out such a function most efficiently is one in which the scalenus medius contracts sufficiently to displace the first thoracic and eighth cervical nerves but not enough to elevate the first rib.

4. *Scalenus medius muscle.* The sites of origin included the posterior tubercles of the transverse processes of the cervical vertebrae from the third to the seventh inclusive. The body of the muscle lay posterior to the roots and trunks of the brachial plexus in all dissections (Figs. 1, 5, 6, and 10b). Its usual insertion was to the superficial surface of the first rib from near the tubercle of the rib to within a short distance of the attachment of the scalenus anticus (Fig. 14b). The average length of the interval between the insertions of the scalenus anticus and medius muscles in 43 male bodies dissected was 7.7 mm. on the right and 7.8 mm. on the left. In 5 cases, the neighboring borders of the scalenus anticus and medius muscles were contiguous or overlapped. The length of this interval varied up to 18 mm. on the right and 19 mm. on the left. In 13 female bodies dissected the same interval averaged

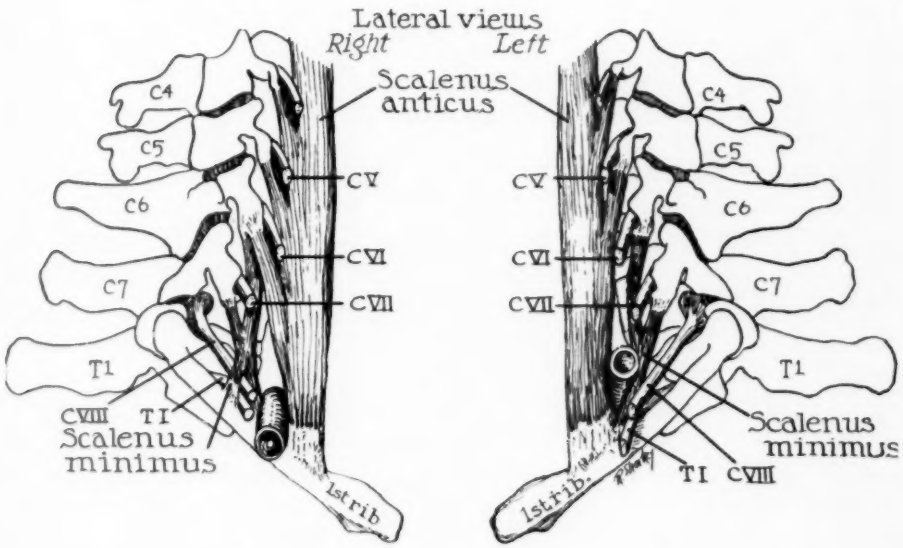

FIG. 13—(A) Usual relations of scalenus minimus to anticus, adjacent spinal nerves, subclavian artery and first rib. (B) Unusual relations of scalenus anticus and minimus to lower components of brachial plexus and to subclavian artery.

6.6 mm. on the right, with a maximum of 13 mm. The average on the left was 6.5 mm. with a maximum of 12 mm. One body revealed an approximation of the adjacent borders of the scalenus medius and anticus.

Although the distance between the insertions of the scalenus anticus and medius muscles, as a rule, was approximately equal on the two sides, in one case there was a 10 mm. difference. The variable relationship between the insertions of the scalenus anticus and medius muscles is demonstrated in Figures 4, 5, 6, and 8. The relationship most commonly seen is that shown in Figure 6. Here a distance of 8 mm. separated neighboring margins of the scalenus anticus and medius muscles. Figures 5 and 8 illustrate scalenus

medius muscles more strategically located to produce symptoms referrable to the brachial plexus.

The effectiveness with which the scalenus medius muscle functions in raising the rib is to a large extent dependent on the size of the muscle and the distance of its insertion from the point about which the rib rotates as it is raised. To estimate the variations in this function of the muscle, measurements were made of the distance between the articulation of the tubercle of the first rib with the first thoracic transverse process and the anterior extent of the insertion of the muscle. In the 43 male bodies dissected the distance varied from 6.7 to 3.4 cm. with an average of 4.9 cm. on the right and from 6.8 to 3.2 cm. with an average of 4.9 cm. on the left (Fig. 14a). In the 13 female bodies dissected the same measurement averaged 4.7 cm. on the right and 4.5 cm. on the left. In this group, the distance ranged from 6.1 to 3.5 cm. on the right and from 5.9 to 3.2 cm. on the left.

The distance between the point of emergence of the first thoracic nerve from the intervertebral foramen and the point at which it crosses the scalenus medius muscle is an index of the amount of traction which may be exerted upon the nerve with contraction of the muscle. This distance was established approximately by measuring the interval between the head of the second rib and the anterior point of attachment of the scalenus medius to the first rib. In the 43 male bodies dissected, the distance averaged 4.0 cm. on each side (Fig. 14a). This interval ranged, on the right, from 2.5 cm. to 5.2 cm. and on the left from 2.7 cm. to 6.2 cm. In the 13 female bodies dissected, this distance averaged 3.5 cm. on each side. It varied, on the right, from 2.5 cm. to 5 cm. and on the left from 2.7 cm. to 3.8 cm.

In practically all dissections, the lower trunk of the brachial plexus rested on the inferior portion of the anterolateral margin of the scalenus medius muscle as it descended into the upper extremity, regardless of the relation between the attachments to the first rib of the scalenus anticus and medius (Figs. 4, 5, 6, 7, 8, and 15a and b). In those bodies in which the distance between the articulation of the tubercle of the first rib with the transverse process and the anterolateral margin of the scalenus medius muscle and the distance between the latter point and the head of the second rib are relatively great, the situation is optimal for irritation to the brachial plexus with spastic contraction of the scalenus medius muscle (Fig. 5). In this instance the former measurement was 6.4 cm. and the latter 5.8 cm. Analysis of our data reveals that such a relationship of the scalenus medius is indicated by approximation or overlapping of the adjacent margins of the scalenus anticus and medius muscles (Figs. 4, 5, and 10a). The anterolateral border of the spastically contracted scalenus medius muscle may act as a sharp ridge over which the component roots of the brachial plexus, especially the seventh and eighth cervical and the first thoracic roots, are drawn by the normal activity of the upper extremity. The angulation of these nerves over the anterolateral border of the scalenus medius muscle is accentuated by retraction of the

upper extremities such as in carrying a pack on the back. With contraction of the scalenus medius, the lower trunk of the brachial plexus may be transferred to a location in more direct contact with the first rib. This position is made more traumatic to the nerves because of the elevation of the rib by the activity of both the scalenus medius and anticus muscles. It should be particularly emphasized that the lower portion of the anterolateral margin of the scalenus medius frequently presents a marked concavity in which the lower trunk of the brachial plexus lies. This is well illustrated in Figure 4. Such a relationship allows for maximal displacement of the lower trunk of

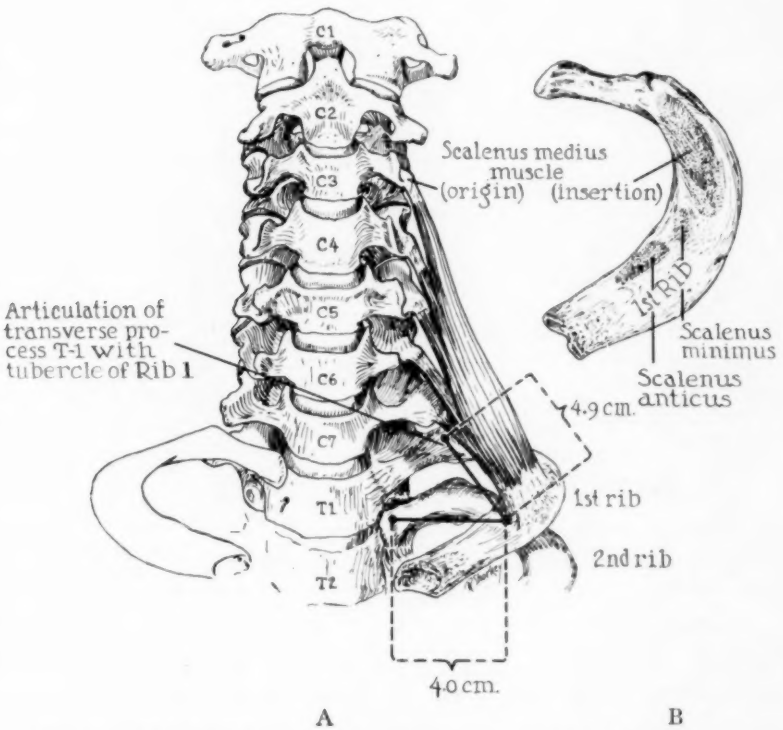

FIG. 14.—(A) Anterior view of scalenus medius and related bony structures. Average distance of the most anterior point of insertion of scalenus medius from the tubercle of the first rib and the head of the second rib as determined in 43 male bodies is indicated. (B) Superior surface of first rib showing usual relations of insertions of scalenus anticus, minimus and medius.

the brachial plexus from its usual position with spastic contraction of the scalenus medius muscle. The scalenus medius does not have as great a mechanical advantage as the scalenus anticus in raising the first rib because of its being attached to the rib closer to the point about which the rib rotates as it is elevated. However, the proximity of the attachment of the scalenus medius to the articulation of the tubercle of the rib with the vertebra allows it to cause a greater upward excursion of the rib as compared with the range

of movement of the rib caused by a contraction of equal strength by the scalenus anticus. The greater size of the scalenus medius suggests that it may be a more important factor in raising the rib than the scalenus anticus. It should also be noted that the scalenus medius usually has an extensive attachment to a cervical rib when the latter is present and frequently the scalenus anticus has none.

5. *Components of brachial plexus.* Although the structure of the brachial plexus varies, it has not been apparent in this series of dissections that the size of the roots of the plexus or their relations with nerves of adjacent segments varied sufficiently to justify the significance which has been attached

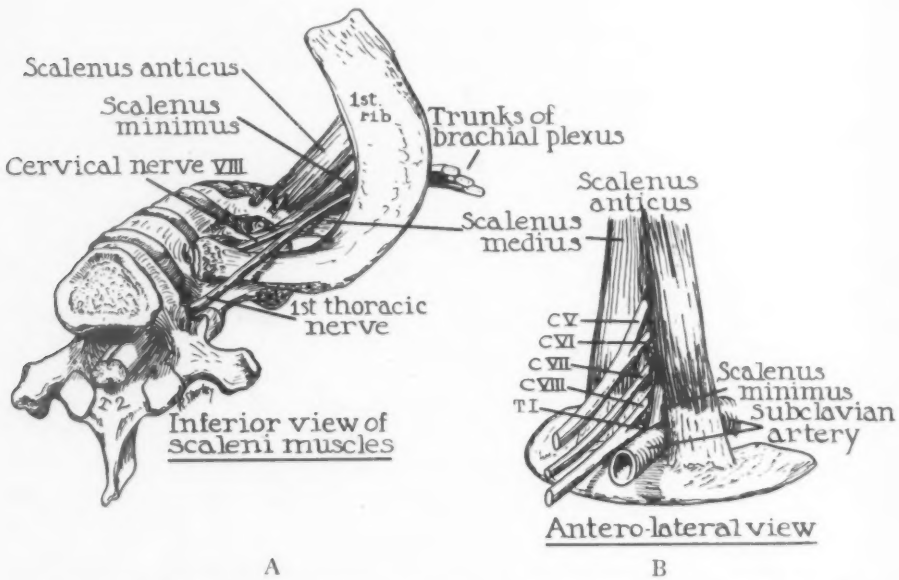

FIG. 15.—Inferior view of scalenus anticus, minimus and medius showing relations of the eighth cervical and first thoracic nerves. (B) Anterolateral view of supraclavicular area showing usual relations of scalenus anticus, minimus and medius to each other and to the adjacent nerves and the subclavian artery.

to "prefixed" and "postfixed" plexuses. The addition to the upper or lower components of a considerable number of fibers would result in a very small increase in the caliber of the roots. The variation in contributions of fibers from segments above or below the fifth cervical or first thoracic was not found to produce relations of apparent importance.

CONCLUSIONS

This series of dissections has demonstrated several factors which seem of importance in the production of the syndrome of the scalene muscles. These are: 1) elevation of the first rib by the activity of the scalenus anticus and medius muscles aided by the scalenus minimus muscle, when the latter is present, with irritation to the lower components of the brachial plexus, 2) contraction of the "posterior" components of the scalenus anticus muscle with

compression of the immediately adjacent nerve root or the subclavian artery, and 3) traction of the components of the brachial plexus, especially the seventh and eighth cervical and first thoracic nerves, across the anterolateral margin of a spastic scalenus medius muscle. A lesser factor is the trauma which may result from the scalenus minimus muscle or vertebrocostal ligament functioning as the anterior jaw of a vise in which the lower trunk of the brachial plexus may be trapped.

It is impossible for the main body of the scalenus anticus muscle, that is, that portion arising from the anterior surfaces of the cervical transverse processes, to compress directly the components of the brachial plexus. This part of the muscle is important in the syndrome only through its activity in elevating the first rib and in serving as a rigid structure against which the displaced subclavian artery may be compressed. However, direct compression of the fifth, sixth, and seventh cervical nerves, especially the latter two, may result from contraction of the bundles of muscle fibers which arise from the inferior and posterior aspects of the cervical transverse processes and join the main body of the scalenus anticus muscle. Although the presence of such bundles of muscle fibers is common, their size and relation to the adjacent nerve and to the subclavian artery are variable. In those cases in which the relation of the bundle of muscles to the nerve is such that the leverage exerted by the muscle is optimal, it is obvious that even a small bundle of muscle fibers might cause sufficient local ischemia of the nerve to produce symptoms.

An unusually large scalenus medius muscle not only may elevate the rib to a greater degree but forms a more prominent ridge across which the lower components of the brachial plexus may be drawn when the muscle is in spasm. The degree of traction exerted on the components of the plexus is also related directly to the distance which this muscle extends anteriorly along the first rib. If the insertion of the scalenus medius approximates that of the scalenus anticus muscle, the situation is most favorable for the scalenus medius to cause symptoms. Traction of the artery across the edge of the muscle or across the first rib may cause alterations in the volume of the pulse as measured at the wrist.

It is possible that the upper extremity may assume a relatively low position and the thoracic cage a relatively high position because of atony or poor development of the muscles of the shoulder girdle and abdomen. However, it seems doubtful that this relationship is ever changed sufficiently by such phenomena that the lower trunk of the plexus would be irritated by being drawn across the first rib or an atonic scalenus medius muscle. It is apparent, on the other hand, that the presence of such a set of circumstances would make one more susceptible to the development of symptoms indicative of trauma to some or all components of the brachial plexus if the scalene muscles were spastically contracted.

We wish to minimize the probability that pure anatomic relations frequently by themselves initiate such muscle spasm. Instead, we desire to stress that the presence of certain anatomic relationships mentioned in this paper may make one considerably more susceptible to the development of symptoms in the presence of scalene muscle spasm. Anterior scalenotomy possibly too frequently has constituted the treatment of only one of the manifestations of a more serious disease.

We believe that surgical treatment of the syndrome of the scalene muscles should include resection of the major portion of the scalenus anticus and of the scalenus minimus or vertebrocostal ligament when either of the latter is present. In addition, if it is apparent that the lower trunks of the brachial plexus may be traumatized by angulation across the anterolateral border of the scalenus medius, as is suggested by the approximation of its insertion to that of the scalenus anticus, the portion of the scalenus medius immediately posterior to the lower trunks of the plexus should be resected.

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THE LOCAL INJECTION OF PENICILLIN IN ACUTE CIRCUMSCRIBED INFECTIONS

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DIRECT LOCAL INJECTION OF PENICILLIN is an effective and economical method of administering this therapeutic agent in acute localized infections caused by organisms sensitive to this antibiotic. To date penicillin has proved to be the most effective agent against staphylococcic and streptococcic infections. It may be given intravenously, intramuscularly, applied topically, or injected directly into an infected area. The regional injection of penicillin in acute local infections is not new. Florey,[1] Cutler,[2] Rose and Hurwitz,[3] Peck,[4] Sophian,[5] Fisher,[6] and others have employed this technic with excellent results.

The purpose of this report is to record the observations and results obtained by the regional injection of penicillin in over three hundred cases of acute localized infections in various parts of the body. This work was initiated in 1943 on a septic surgical ward of an Army regional hospital, and continued on the surgical out-patient services of Touro Infirmary and of Charity Hospital of Louisiana at New Orleans. The results obtained were so highly satisfactory that it is surprising that this method of administration has not gained in popularity.

Acute infections may be divided for practical purposes into two clinical types:[7] (1) acute infections which do not cause death of tissue, such as septicemia and cellulitis and (2) acute infections causing suppuration and death of tissue, as seen in boils and carbuncles. In the absence of suppuration or death of tissue, acute infections are superficial and spread over a wide area, relatively unconfined by a wall of inflammatory tissue. In contrast, where suppuration and death of tissue have occurred, a localized area of gangrene is surrounded by a zone of granulation tissue which separates the living from the dead tissue and which circumscribes the infection and prevents its spread, but which also acts as a barrier to a free circulation into the diseased area. Because of these differences, the response to any form of therapy is not the same in these two types of acute infection.

It has been shown that the results of parenteral therapy with penicillin may vary considerably in the two types of acute infection. The results in acute infections in which there is no death of tissue are quite dramatic, while in acute localized infections, with suppuration, the results are not only less dramatic but at times even discouraging. If penicillin therapy is to be effective, the infecting organisms must be susceptible to the antibiotic and an adequate

concentration of the drug must be obtained in the tissue in which the bacteria are imbedded. Because of the impenetrable inflammatory barrier surrounding a localized area of gangrene, circulation to this area is impaired and penicillin, when given parenterally, does not reach the diseased areas in sufficient concentration to be of any value.

Penicillin has several properties that give it distinct value as an antibacterial agent, for local application. It is active against most of the organisms responsible for acute local infections. It is active in high dilutions. It is not inhibited by exudates, and it is non-toxic when given either locally or parenterally.

In view of these facts, it seemed to us that the most suitable method of administration of penicillin in acute localized infections should be direct injection into the infected area. By this means a high concentration and a deep even distribution of the drug at the point where it was needed could be assured. The injections should be repeated often enough to ensure prolonged contact, thereby killing or inhibiting the growth of bacteria, so that the natural defenses of the body could complete the rest of the destruction and proceed with the process of repair.

The response obtained by this method of treatment, when compared with results of the general administration of penicillin, was so striking that it seems worthwhile to direct further attention to this method of treatment.

METHOD OF TREATMENT

Three cubic centimeters of distilled water are injected into the bottle containing 100,000 units of penicillin, making a dilution of approximately 33,000 units to the cubic centimeter. The size of the lesion determines the amount of the solution to be injected. Too much tension in the infected area may break down the barriers that the body has set up to localize the infection and must be avoided. This is a matter of judgment. Small lesions require 0.5 to 1 cc. at each injection, while larger ones, such as a carbuncle, may require 4 cc., or even more. Approximately 1 cc. is given for the average localized abscess. The required amount is aspirated from the bottle containing the solution and the remainder kept in the ice box for injection on the following day, as the potency of refrigerated penicillin in solution is maintained for approximately twenty-four hours.

The injection is made with a 24-gauge hypodermic needle into the most dependent area of the abscess. Without entirely removing the needle, the operator makes several injections into different areas of the lesion in order to insure an even distribution of the drug. Usually spontaneous evacuation of pus occurs during the injection, depending upon the stage of the infection. If the abscess is superficial and pointing, this occurs practically all the time. In cases in which the abscesses are fluctuant, they are aspirated with a larger needle immediately before the injection of the penicillin solution. In carbuncles the injections are made between the areas of pointing, and the needle is usually inserted deeper than in the localized abscesses.

Following the injection a dry sterile dressing is applied. For several reasons it is desirable to keep the infected area closed. (1) This keeps the penicillin solution in contact with the infecting organisms. (2) It is important to obtain as high a concentration as possible in the diseased area, for in the early stages of infection there are some strains of staphylococci which are resistant to low concentrations of penicillin but are susceptible to the higher concentrations. (3) The danger of infection of the wound by secondary invaders which may produce penicillinase is minimized.

The injections are usually quite painful, the degree of pain varying with the density of the tissues and the volume of the fluid injected. However, the pain does not persist more than 4 to 6 hours.

Some increased redness is usually noted on the day following the injection. At that time another injection is made in the same manner as the first. On the third day the degree of resolution noted is quite surprising.

In about one-fifth of the furuncles only one injection was necessary; the others required 2. Most were entirely healed on the fourth day. The carbuncles required 3, and occasionally 4, injections, and were healed on the tenth day. In a large number of abscesses there was complete absorption without any external drainage.

RESULTS

Carbuncles.—There were 24 carbuncles in this series: 8 on the posterior aspect of the neck, 10 on the upper back, 2 on the buttocks, 1 on the right anterior lateral abdominal wall, and 3 on the thigh. The average number of injections given on successive days was 3. The average number of days required for healing was ten.

These results are in marked contrast to those observed following surgical procedures. An average of 43 days was required for healing following incision and drainage in a series recently operated by Maes and Herringman.[8, 9] Extremely gratifying, in addition to the rapid healing time, was the cosmetic result obtained. There was no loss of skin and there were no deforming scars, as seen following surgical intervention.

A short control series was run in this group. Two patients with carbuncles on the neck were given 30,000 units of penicillin parenterally every three hours for seven days. At the end of this period both patients still had large carbuncles with many areas of drainage. It was six weeks following incision and drainage before healing took place. Two carbuncles on the back of the neck were injected locally with 100,000 units of penicillin in 3 cc. of distilled water daily for three days. In addition, 30,000 units of penicillin were administered intramuscularly every three hours for ten days. The response was dramatic. The carbuncles seemed fairly to melt away and were entirely healed in ten days. Two carbuncles, one on the back of the neck, the other on the buttocks, were treated solely by local injection of 100,000 units of penicillin in 3 cc. of distilled water daily for three days. The results were equally as good as in the group which had been given penicillin parenterally as well as locally.

In the two patients who received penicillin parenterally only, it is doubtful that the drug reach the infected areas in sufficient concentration to be of any definite value. Because of the inflammatory barriers surrounding the infection and the lack of circulation to the necrotic center, the antibiotic could not be expected to reach the bacteria imbedded in the slough and sterilize it. In contrast to the difficulty and expense of the maintenance of a high concentration of penicillin by parenteral administration over a period of many days or weeks, local injections offer a suitable and efficient alternative.

Furuncles.—Furuncles formed the largest group in this series of cases. Eighty-seven per cent responded favorably to this form of therapy; 13 per cent required incision and drainage.

Breast Abscesses.—Two abscesses of the breast were seen. They were both superficial, located near the nipple, and fluctuant. They were aspirated and injected with 60,000 units of penicillin in 2 cc. of distilled water on two successive days. Both were healed on the fifth day.

Axillary Furunculosis.—There were 10 cases of axillary furunculosis. Seven patients had multiple lesions. All responded favorably and there were no recurrent "crops" as often seen following incision and drainage. The average time for healing, following 2 successive injections, was five days.

Cellulitis.—While a fairly large number of cellulitides were seen, only a few were treated by local injections and this procedure was soon discontinued. These infections are superficial and not well localized. Any increased tension in them will cause the infection to spread. This happened in one of our patients when we first began this form of therapy. A young man was seen with an area of cellulitis measuring approximately 5 x 6 cm. on the ventral aspect of the right upper forearm. The are was injected locally with 60,000 units of penicillin in 2 cc. of distilled water. The following day the area of inflammation had spread to an alarming proportion. He was admitted to the hospital and, with the administration of penicillin intramuscularly, the lesion cleared in a short time. This type of infection responds rapidly to parenteral therapy and should be so treated.

CONTRAINDICATIONS

Local injection of penicillin is not recommended in infections in the dangerous areas of the face, in cellulitides, and in bone felons.

COMMENT

It is not the purpose of this report to leave the impression that this form of therapy should be used in all types of acute localized infections. It should be reserved for the more serious ones and for the lesions so located that surgical procedures may produce a bad cosmetic result. It is useful when surgical intervention has proved to be inadequate. In well localized infections that are fluctuant, simple aspiration or incision and drainage are the procedures of choice. Surgical judgment should be exercised in each individual case.

SUMMARY

(1) The technic and the results of the local injection of penicillin in acute circumscribed areas of infection in over three hundred ambulatory patients are presented.

(2) Experience with this method of local therapy with penicillin has demonstrated that it is safe, effective and economical. There were no complications.

(3) Because of the impermeable inflammatory barrier surrounding an acute localized infection, penicillin, when given parenterally, may not reach a sufficient concentration in the affected area for therapeutic effectiveness.

(4) By local injection it is possible to reach a concentration in the infected area far in excess of the highest levels obtained by intramuscular administration.

(5) Following injection directly into the affected tissue, there is almost immediate improvement and recovery is established in a few days.

(6) Extremely gratifying, in addition to the rapid healing time, is the cosmetic result obtained. There is practically no loss of skin and no deforming scars are seen as usually found following surgical intervention.

(7) This procedure is not recommended for the treatment of the cellulitides, for infections in the dangerous areas of the face, or for bone felons.

(8) Surgical judgment must be exercised in each individual case.

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TEMPORARY FAILURE OF GALLBLADDER VISUALIZATION BY CHOLECYSTOGRAPHY IN ACUTE PANCREATITIS

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DURING A FIVE-YEAR PERIOD intravenous cholecystograms were done on 28 patients with acute pancreatitis. In all cases the initial cholecystography was performed during the acute phase of the disease (Table I). In 12 patients the gallbladder visualized and in 16 patients the gallbladder failed to visualize at the initial cholecystography. Six of the latter group had cholecystograms after the signs and symptoms of the disease had subsided, which revealed a normally visualizing gallbladder (Fig. 1 and 2). In five cases cholecystography was not repeated. The remaining five cases in which the gallbladder did not visualize during the acute stage of pancreatitis were subjected to laparotomy; the gallbladder appeared grossly normal in all cases, and was within normal limits by microscopic examination in the three cases in which the normal appearing gallbladder was removed (Fig. 3 and 4). Patients with evident cholecystitis and pancreatitis were excluded from this case study.

The eleven cases of acute pancreatitis with temporary failure of gallbladder visualization in which subsequent cholecystography or operation demonstrated an essentially normal gallbladder are summarized as follows:

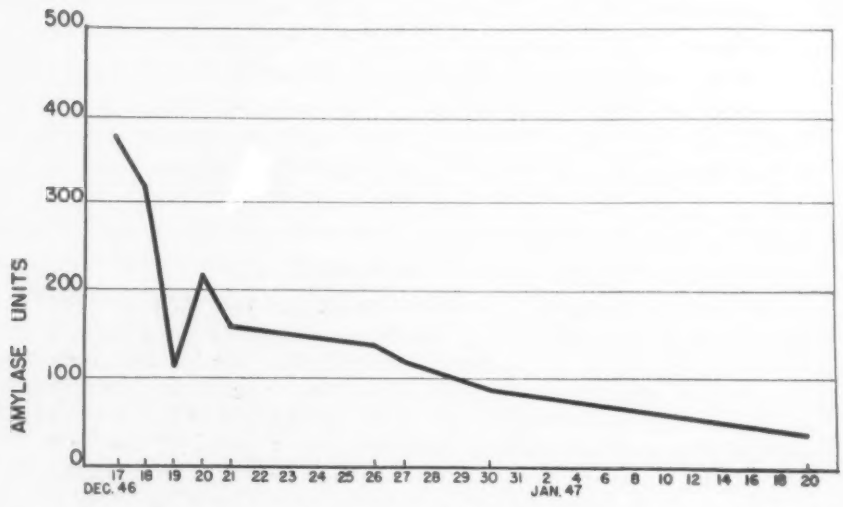
Case 1: A man 52 years of age complained of intermittent abdominal pain, nausea, and vomiting of six days' duration. Examination revealed diffuse abdominal tenderness most marked in the epigastrium. The highest blood serum amylase reading was 922 Somogyi units. Liver function tests were not done. All symptoms and signs of the disease subsided under conservative treatment over a period of four days. The gallbladder failed to visualize by the intravenous iodekon method on the sixth day of the disease. However, on the twenty-third day, 13 days after the acute episode of pancreatitis had subsided, intravenous cholecystography revealed a normal gallbladder visualization.

Case 2: During a period of four months a woman 68 years ot age had three episodes of nausea, vomiting, and epigastric pain radiating to the back and shoulders. Her most recent illness began seven days before examination. The epigastrium and right lower abdomen were tender. The highest serum amylase reading was 502 Somogyi units. Icterus index, blood serum proteins, and sodium benzoate conjugation were within the limits designated as normal. The gallbladder failed to visualize by the intravenous iodekon method on the seventh day of the last acute episode of pancreatis. The acute symptoms and signs of the disease subsided over a period of six days under conservative management. On the 19th day, six days after the acute pancreatitis subsided, the gallbladder visualized normally by intravenous cholecystogram.

Case 3: A man 32 years of age gave a history of two episodes of cramping epigastric and generalized abdominal pain. Also there was a history of alcoholism. The more recent attack began seven days before examination. There was a moderate degree of tenderness in the epigastrium. The highest blood serum amylase reading was 449 Somogyi units. Bromsulphalein excretion, cephalin flocculation, blood serum proteins, prothrombin time and serum cholesterol were within the limits ordinarily designated as normal. The gallbladder failed to visualize by the intravenous iodekon method on

the seventh day of the recent episode. The acute symptoms and signs subsided with conservative treatment over a period of twenty-four hours. On the 16th day, nine days after the acute pancreatitis subsided, the gallbladder visualized normally following the intravenous administration of iodekon.

Case 4: A man 32 years of age had four attacks of nausea, vomiting and epigastric pain over a period of three years. Examination three days after onset of the most recent attack revealed diffuse abdominal tenderness, most marked in the epigastrium. The highest blood serum amylase reading was 582 Somogyi units. Blood serum cholesterol, proteins and icterus index were within the limits of normal. The gallbladder failed to visualize by the intravenous iodekon method on the third and on the fifth days of the acute illness. The symptoms and signs of the acute illness subsided rapidly under conservative treatment. On the 27th day following the onset of the illness the gallbladder visualized normally by intravenous cholecystography.



(5) E.D.

FIG. 1. Case 5. Acute pancreatitis. Blood serum amylase. Determinations expressed in Somogyi units.

Case 5: A man 29 years of age had two attacks of epigastric pain with nausea and vomiting in a period of four years. Two days after the beginning of the more recent attack examination revealed tenderness in the epigastrium and periumbilical regions. The highest blood serum amylase reading was 376 Somogyi units. With conservative management the symptoms and signs of the disease subsided over a period of four days. The gallbladder failed to visualize by the intravenous iodekon method on the second day of the acute illness, but visualized normally on the 38th day, 32 days after the signs and symptoms of acute pancreatitis had subsided.

Case 6: A man 55 years of age complained of epigastric and left subcostal pain of two days' duration. There were tenderness and spasm in the epigastrium and lower right abdomen. Maximum blood serum amylase reading was 264 Somogyi units. Icterus index and blood serum proteins were within the limits of normal. Over a period of two days the signs and symptoms of the disease subsided with conservative treatment. On the second day of the acute illness the gallbladder failed to visualize by the intravenous iodekon

TABLE I.—*Cholecystography in 28 Patients with Acute Pancreatitis*

	Number of cases
Normal gallbladder visualization during acute pancreatitis	12
Temporary failure of gallbladder visualization during acute pancreatitis; normal visualization after disease subsided	6
Temporary failure of gallbladder visualization during acute pancreatitis; normal gallbladder found at operation	5
Failure of gallbladder visualization during acute pancreatitis; subsequent visualization or operation not done	5
TOTAL	28

method, but it visualized normally on the 23rd day, 19 days after the acute signs and symptoms of pancreatitis had subsided.

Case 7: A woman 43 years of age had repeated attacks of epigastric and right upper abdominal pain over a period of two weeks. Examination two days after the onset of the most recent episode revealed tenderness in the epigastrium. The maximum blood serum amylase reading was 1100 Somogyi units. Liver function tests were not done. At this time the gall bladder failed to visualize by the intravenous method. Laparotomy on the same day revealed an acute pancreatic edema but the gallbladder appeared perfectly normal. The patient promptly recovered but had a recurrence one month later.

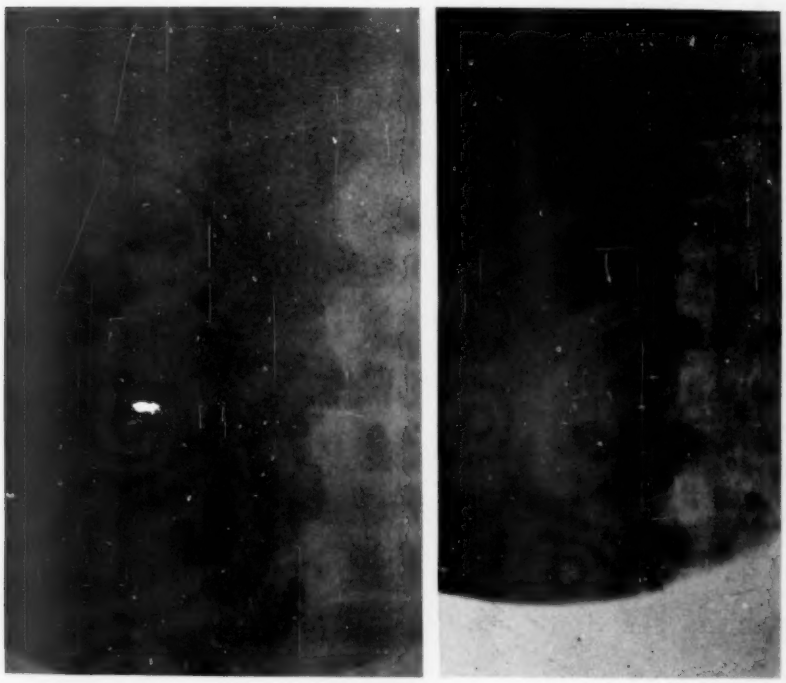


FIG. 2.—Case 5. Intravenous cholecystography. Left, on second day of acute pancreatitis gallbladder did not visualize. Right, on 38th day, 32 days after acute pancreatitis subsided, normal gallbladder visualization.

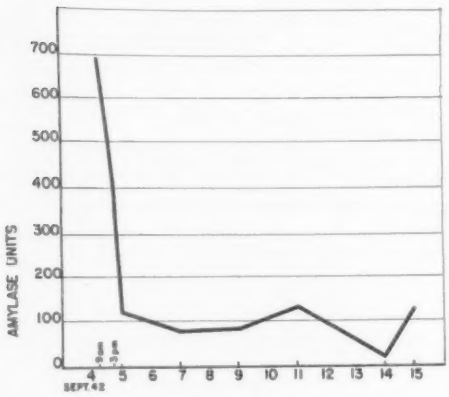


FIG. 3.—Case 9. Acute pancreatitis. Blood serum amylase determinations expressed in Somogyi units.

Case 8: A man 43 years of age complained of epigastric and right lower abdominal pain with nausea and vomiting of two days' duration. The patient appeared very acutely ill and there was spasm and tenderness throughout the upper abdomen. A serum amylase and liver function determination were not done. The gallbladder failed to visualize by the intravenous iodekon method. Laparotomy performed on the second day of the illness revealed an acute hemorrhagic pancreatitis. The gallbladder appeared normal. The patient died shortly after the operation.

Case 9: A man 47 years of age complained of epigastric pain, nausea and vomiting of six days' duration. Examination revealed tenderness and rigidity in the upper abdomen. The maximum blood serum amylase reading was 690 Somogyi units. The sodium benzoate conjugation test was within normal limits. The gallbladder failed to visualize by the intravenous iodekon method on the sixth day of the acute illness. Symp-

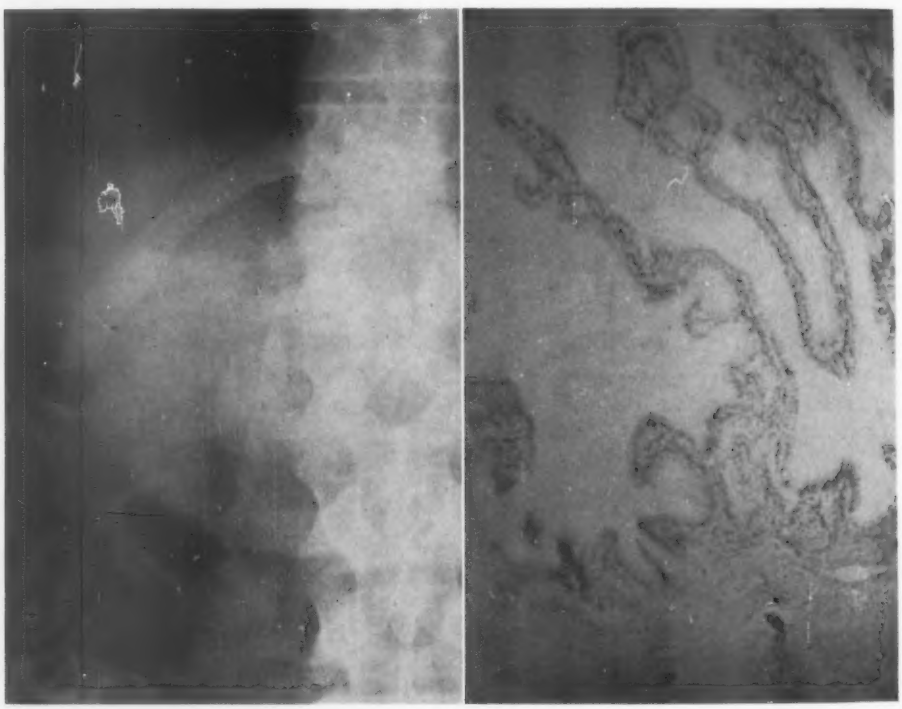


FIG. 4. Case 9. Left, the gallbladder does not visualize by intravenous cholecystogram on sixth day of an attack of acute pancreatitis. Right, normal histologic appearance of the wall of the normal appearing gallbladder removed at operation.

toms of the acute illness subsided in 24 hours. Laparotomy revealed an indurated pancreas. The gallbladder was removed and found to be grossly and histologically normal. The patient recovered promptly.

Case 10: A man 50 years of age complained of nausea, vomiting, and epigastric pain radiating to the back of five days' duration. There was tenderness to palpation deep in the epigastrium. The maximum blood serum amylase reading was 553 Somogyi units. The gallbladder failed to visualize by the intravenous iodekon method. Sodium benzoate conjugation and prothrombin time were normal. The acute symptoms and signs of the disease subsided in two days. Laparotomy revealed an indurated pancreas. The liver and gallbladder appeared to be normal. Cholecystectomy was performed. Gross and histological examination revealed a perfectly normal gallbladder. The patient recovered.

Case 11: A man 55 years of age complained of severe epigastric and generalized cramping abdominal pain of ten days' duration. Examination revealed tenderness and rebound tenderness in the upper abdomen. The blood serum amylase was 265 Somogyi units. The icterus index and Rose Bengal excretion tests were within normal limits. The gallbladder failed to visualize by the intravenous iodekon method. The acute symptoms of the disease subsided over a period of three days. At laparotomy the pancreas appeared edematous and indurated; the liver and gallbladder appeared normal. Cholecystectomy was performed. The gallbladder was normal by gross and histological examination. The patient recovered.

From this group of cases it appears that in some patients with acute pancreatitis, the ability of the apparently normal gallbladder to concentrate iodekon was lost temporarily during the acute phase of the illness. No evidence of impairment of hepatic function was found in those cases in which liver function tests were done, and none of the patients were jaundiced. Elman[1] mentions this phenomenon but does not explain it. The reason for temporary failure of gallbladder visualization by cholecystography in this selected group of patients with acute pancreatitis is not apparent at present.

SUMMARY

In a selected group of 28 patients who had cholecystograms made during the acute phase of illness with acute pancreatitis the gallbladder visualized normally in 12 cases and failed to visualize in 16 cases. In six patients in the latter group the failure of the gallbladder to visualize during the acute illness was temporary, and additional cholecystograms made after the acute pancreatitis had subsided gave normal visualization of the gallbladder. In five other patients the gallbladder failed to visualize during the episode of acute pancreatitis but the gallbladder was found to be normal at operation. In the remaining five cases in which the gallbladder did not visualize during acute pancreatitis no follow-up cholecystography or operation was done.

Explanation of this phenomenon of temporary failure of visualization of the apparently normal gallbladder in this selected group of patients with acute pancreatitis is not apparent.

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A DEPENDABLE METHOD FOR CONSTANT INTRAVENOUS THERAPY IN INFANTS USING POLYETHYLENE TUBING

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MAJOR SURGICAL PROCEDURES in infants and small children present many special problems, not the least of which is the technical difficulty of administering fluids and blood intravenously. The loss of 100 cc. of blood in a small infant during an operation may be unavoidable. This amount, though negligible in a large child or adult, represents a significant percentage of the blood volume of a small infant and must be quickly replaced.

It has been common practice for many years at The Children's Hospital to have a constant intravenous infusion running before any major surgical procedure is undertaken either in infants or children. In the past this has been accomplished by making a small incision over the medial malleolar vein, isolating it, and inserting into it a blunt No. 19 or No. 20 gauge needle which can be tied in place. This method has been satisfactory in larger children, but in infants it has been difficult at times to place the needle properly in the vein and to maintain its patency when the infant is moved on the operating table or during long operations. Such needles require almost constant attention because the incidence of clotting in the needle is high, particularly in small infants when the fluid must drip slowly before operation. This clotting has often stopped the flow of blood into a vein at a critical point in an operation.

A modification of the method has been sought and preliminary experimentation was carried out on animals before the method to be described below was adopted for use in infants. Myers[1] has described a method of inserting a plastic tubing through a large bore needle in adults for repeated administration of intravenous medication. This method is hardly applicable to infants, in whom the veins are not large enough to accommodate the large needle necessary for the insertion of a tubing. Advantage has been taken of a new plastic, polyethylene (polythene),† which can be made in the form of film or tubing and which is flexible, semi-transparent, tough, light, and easily sterilized. When obtained in absolutely pure form it has been found by Ingraham, Alexander and Matson[2] to be non-irritating to tissues and as well tolerated

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as tantalum, vitallium and methylmethacrylate. Diamond and Thomas[3] have used polyethylene tubing in replacement transfusions of newborn infants with *erythroblastosis fetalis*. They have encountered no difficulty with clotting in the tube, which is placed in the umbilical vein of the infant. It has been possible for them to perform replacement transfusions of over 500 cc. by this method.

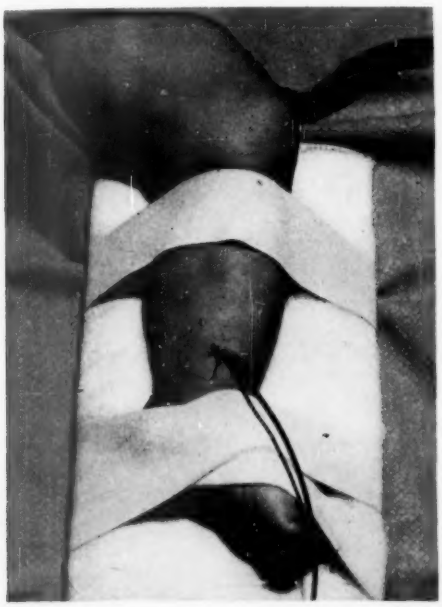

FIG. 1.—Leg of infant secured to padded board with adhesive strips. Polyethylene tube inserted into internal malleolar vein under local Procaine anesthesia. Whole blood running through tube.

TECHNIC

The infant is lightly secured to a wheeled litter in a room adjoining the main operating room. The leg is strapped to a padded board as shown in the accompanying photograph (Fig. 1). The skin is prepared as for any surgical procedure and draped with sterile towels. The region over the internal malleolar vein is infiltrated with 1 per cent procaine. The instruments and drapes supplied for this procedure include gown and gloves, basins for solutions used in preparing the skin, 1 per cent procaine, 2cc. syringe, four hemostats, a pair of small forceps a small scalpel, scissors, a fine nerve hook, silk sutures, gauze sponges, towel clips and a No. 18 needle.

A piece of polyethylene tubing 30-40 cm. in length is provided. Two sizes of tubing are used, one with an outside diameter .067 and an inside diameter of .047 into which an No. 18 needle fits snugly, and a second less frequently used size (outside diameter .050, inside diameter .034) which accommodates a No. 19 gauge needle. The tubing is sterilized by soaking in a 1:1000 aqueous solution of Zephiran for 18 to 24 hours. Attention should be directed to the necessity for filling the lumen of the tubing with the solution and to weighting the tubing to the bottom of the solution pan with a material heavier than water.

An incision 1.0 to 1.5 cm. long is made transversely just lateral to the medial malleolus. If the medial malleolar vein is excessively small or has been previously utilized in other operations, the veins over the radial side of the wrist or in the antecubital space are employed. The tissues are spread, the vein picked up with a nerve hook, and the vein freed from the surrounding tissue for a distance of 1 cm. A silk tie is placed on the vein distally for use in traction. The end of the plastic tubing is bevelled with scissors. A small opening is made

with the scissors and the tubing inserted while traction is exerted on the suture distally. Ordinarily the tubing can be inserted easily 6 to 10 cm. into the vein, but it will usually function satisfactorily if inserted only 1 to 2 cm. It is withdrawn about 1.0 cm. to obviate the possibility of the end of the tubing being lodged against a valve in the vein. A piece of fine silk is then placed around the vein and tubing within it and tied securely. Two silk sutures are used to approximate the skin edges.

A segment of tubing about 25 cm. in length is allowed to extend from the wound and it is secured to the foot and ankle by two pieces of adhesive tape (Fig. 2). The tubing is attached to a needle which in turn is joined to a rubber tubing and buret by means of a syringe with a sidearm or an ordinary glass adapter. A glass drip is incorporated in the rubber tubing so that the rate at which the fluid is running can be accurately determined.

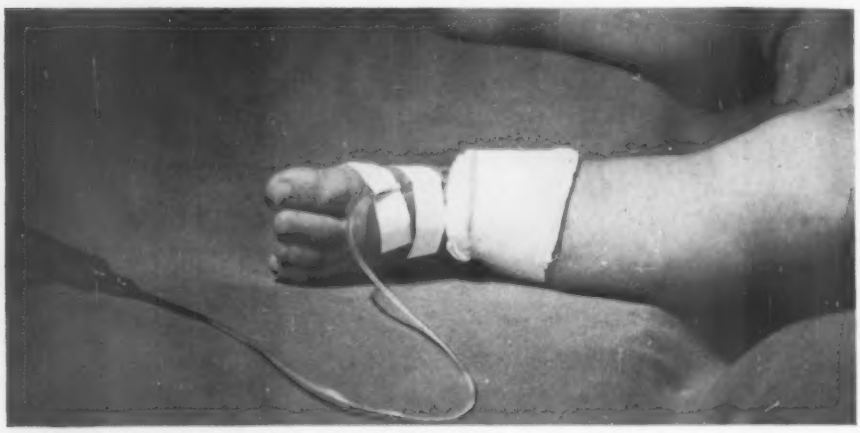

FIG. 2.—Leg removed from restraining board. Transparent polyethylene tube secured to foot by two small pieces of adhesive. Wound covered by sterile dressing. Distal end of tube connected to sidearm syringe of intravenous drip set by No. 18 gauge needle which fits snugly into tube.

The leg is removed from the board to which it was secured during the insertion of the intravenous tubing. It is not immobilized. General anesthesia is then begun and the patient transported to the operating room.

The patient is usually taken to the ward after operation with the intravenous tubing in place. This can be done either with the intravenous solution dripping or with a small syringe attached to the tubing, the tubing irrigated with isotonic saline solution, and the plunger of the syringe held in the closed position with a strip of adhesive (Fig. 3). It is possible to resume the administration of fluids through the tubing several hours later merely by attaching another rubber tube with glass adapter to the plastic tubing. The syringe has been left in place on the plastic tubing as long as 18 hours on several occasions and the administration of fluids resumed again without difficulty.

It has been the usual practice to remove the tubing from the vein within 24 hours after its insertion, but in many instances the tubing has been left in

place 48 hours or more, and in one instance it was allowed to drip continuously for five days. The tubing has occasionally been left in place longer than 48 hours either because of the necessity for administering fluids to a seriously ill infant without further disturbances to the patient, or, during the period of development of the method, to determine its feasibility for prolonged administration of fluids to infants with diarrhea, nutritional disturbances, and those unable to take fluids by mouth. In no instance has blood clotted within the polyethylene tube so that it was impossible to resume the administration of fluids.

DISCUSSION

This method of administering intravenous fluids and blood has been used in over 90 cases on the neurosurgical service since January 1, 1947, and it has

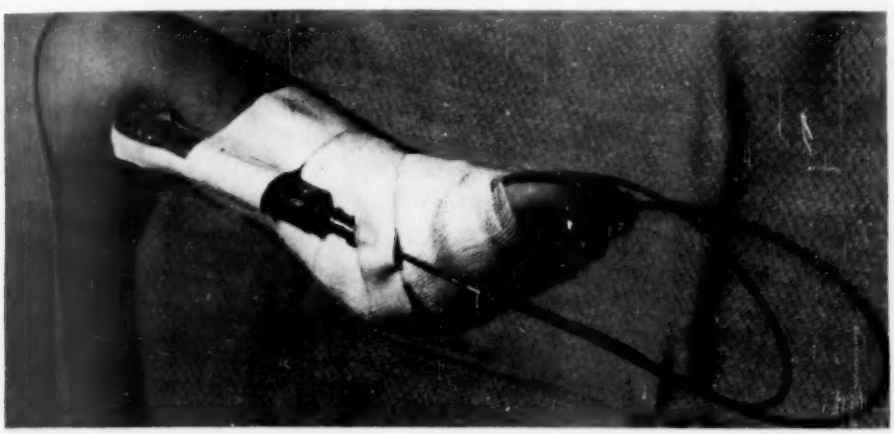

FIG. 3.—After operation the infusion of intravenous fluids may be discontinued for 18-24 hours and started again through the same plastic tube. The tube is irrigated with isotonic saline. Plunger of syringe held in closed position with adhesive to prevent reflux of blood into the tube. Syringe secured to lower leg. Intravenous drip begun again by reconnecting set containing fluid to the plastic tube.

been found to have many advantages over the methods previously employed. The most valuable feature of this method is its dependability. Only once during the six months' period of its use during all major neurosurgical procedures at The Children's Hospital has there been any difficulty with the administration of blood during an operation. In that case the tubing had been inserted through the wall of the vein and was not lying in the lumen. In all other instances it has been possible to administer whatever fluid or blood was necessary, in some cases up to 1500 cc. of blood over a period of less than 45 minutes.

The ease with which the tubing can be placed in the small veins of infants is also a distinct advantage. The tubing is placed in the vein by the house officer on the service before the anesthesia is started. In most cases the house officer has had only a few months of surgical training, but even in inexperienced hands, the insertion of the tubing rarely requires more than a few minutes.

One disadvantage of this method should be mentioned. Although citrated whole blood will run by gravity through the tubing as slowly as desired, it will not run so rapidly as is sometimes needed to replace blood lost during a major operation. It is therefore necessary to pump whole blood by means of a syringe attached to a three-way stopcock in the rubber tubing of the intravenous set. It has been found possible to transfuse large amounts of blood by this means without difficulty. Even if blood does reflux from the patient into the plastic tubing and form a small clot at the end of the tube, it is easy to dislodge the small clot with a syringe filled with saline attached to the needle of the tubing.

The problem of superficial phlebitis following the insertion of any constant intravenous needle or tubing is an ever-present one. In the 90 patients with whom this tubing has been used, eight cases of superficial phlebitis have been observed, all of which subsided rapidly after the tubing was removed. None of them have resulted in further complications or in residual swelling of the leg. In only one case has the superficial phlebitis been found to occur under the 24-hour period, and only four cases developed superficial phlebitis under the 48 hour period. In at least two of these hypertonic solutions such as "Amigen" or 10% dextrose in water were administered. All of the other instances of phlebitis resulted after periods of more than 48 hours and in no case was there evidence of infection in the wound itself, or of any reaction to the tubing. Deep phlebitis did not occur in any of the cases.

The greatest value of the method lies in its dependability during major surgical procedures in infants and the relative simplicity with which it can be employed even by those not extensively trained in surgical technic. If, therefore, the tubing were routinely removed before the end of the 24-hour period after insertion, and if only relatively isotonic solutions and blood were administered, the complication of phlebitis would be practically non-existent.

SUMMARY

1. A technic for administration of fluids and blood intravenously to small infants during surgical procedures has been described.
2. The success of the method depends upon the non-irritating qualities of a new plastic tubing, polyethylene, in which the whole blood shows delayed clotting.
3. The method is dependable and easily employed, even by inexperienced persons.
4. It has been found useful in over 90 major neurosurgical procedures and is of benefit in the administration of fluids during the postoperative period.
5. Superficial phlebitis occasionally develops but in only one case did it develop when the tubing had been in place less than 24 hours, and in only four cases under 48 hours.

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PHLEBOGRAPHY IN THE LOCALIZATION OF INCOMPETENT COMMUNICATING VEINS IN PATIENTS WITH VARICOSE VEINS*

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Since high ligation was first proposed as a remedy for varicosities of the long saphenous system, it has been recognized that this procedure would produce a lasting cure only if the valves of the communicating veins were competent. Various clinical methods have been devised for testing this competency.[1, 2, 3] Although selection of patients for high saphenous ligation is made only after the performance of one or more of these clinical tests, the incidence of postoperative recurrence of varicose veins remains disappointingly large. The failure of high ligation has been attributed by Sherman[4] to incompetence of communicating veins not revealed by the usual tourniquet examinations. He has demonstrated incompetence at operation in cases in which tourniquet tests were negative. It is apparent that a more accurate method of detecting incompetent communicating veins would improve the results of operation for varicosities. It is the intention of this paper to introduce phlebography for this purpose.

METHOD

Each patient with varicose veins is first subjected to the usual clinical examination including Trendelenberg tourniquet tests. If the varicose veins fill below a high thigh tourniquet within 30 seconds, the incompetent communicating veins are localized between two tourniquets.

Next a phlebogram is performed by the following technic. Three tourniquets are placed respectively, just above the malleoli, a few centimeters above the femoral condyles, and as high as possible on the thigh. All three tourniquets are adjusted to hinder but not completely obstruct the flow of blood through the deep veins. The patient is placed in the supine position and a 20 gauge needle introduced into one of the superficial veins on the dorsum of the foot. 30 cc. of 35% diodrast are injected rapidly. Antero-posterior and lateral roentgenograms are taken of the lower leg. The ankle and the low thigh tourniquets are released and an AP plate is taken of the thigh.

The roentgen-ray appearance of incompetent communicating veins varies. Of the two communicators visible in Fig. 1, the lower one (B) may be fol-

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lowed readily from its posterior tibial vein origin to the saphenous vein, whereas the upper communicator is visible only for a short distance beyond its origin.

Communicating veins frequently occur in pairs especially on the lateral aspect of the leg. Actually the paired veins are vena comities of a small artery which is usually dwarfed by the dilated and tortuous veins which accompany it.

It is not necessary to distinguish antero-medial from postero-medial com-

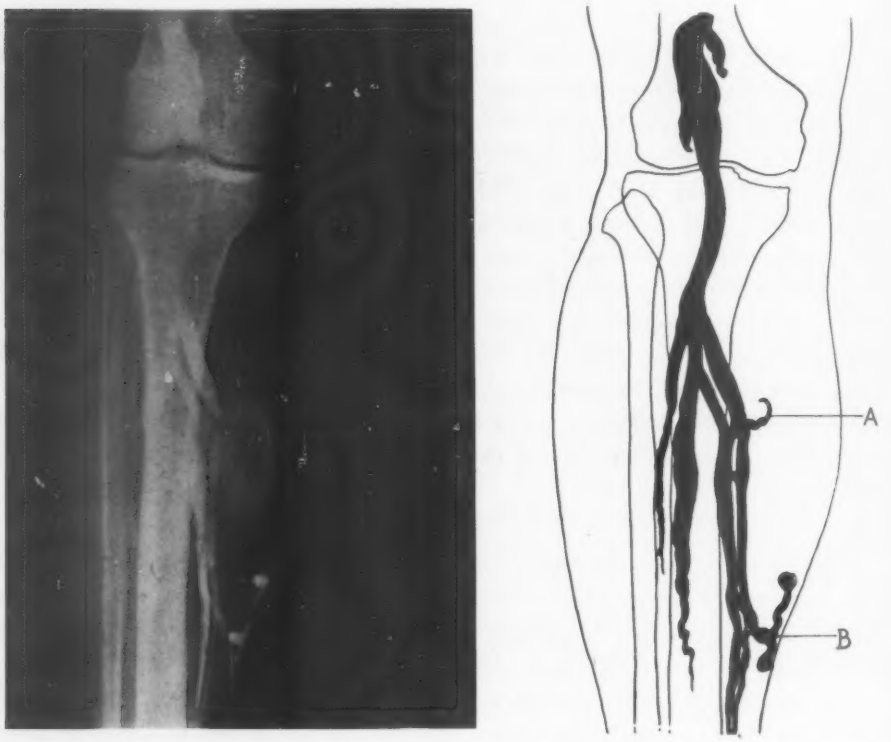

FIG. 1.—Two incompetent communicating veins are readily visible on the medial aspect of the leg, the lower one (B) empties into a dilated superficial varix at a site at which ulcer formation is frequent.

municating veins. However, because of the arrangement of the fascial compartments on the lateral side of the leg, it is desirable to determine whether a particular vein passes behind or in front of the fibula. By correlating the lateral with the antero-posterior roentgen-ray exposure it is possible to localize the veins fairly accurately.

Incompetence is not often encountered in the veins which connect the superficial and deep venous systems in the thigh. Furthermore the venous connections between the two systems are of the nature of perforating veins rather than true communicating veins. In addition to the anatomic patterns described by Sherman on the medial aspect of the thigh, there also seem to

be perforating veins on the lateral aspect which empty into the profunda femoris.

Two sources of error are demonstrated in Fig. 5. Incompetent communicating veins will often not be detected if there is incomplete filling of the deep veins with which they communicate. On the other hand superficial veins which have been filled from an incompetent communicator above or below may overlap the deep system so as to simulate perforating or communicating veins.

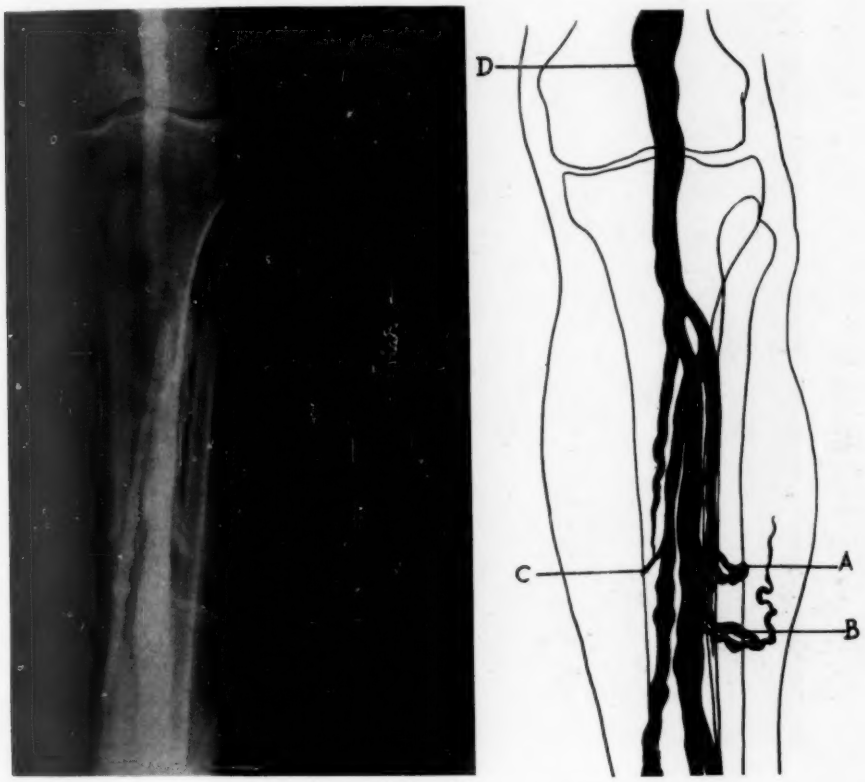

FIG. 2.—(A) and (B) each denote a pair of dilated lateral communicating veins and (C) a medial vein which were confirmed at operation. One medial communicator was found by stripping at (D) but did not appear in the phlebogram or by tourniquet examination.

In order to test the comparative accuracy of the two methods used for localizing incompetent veins, a rather radical operative procedure is carried out. After the conventional high saphenous vein ligation, a Sherman[5] type of stripping is performed. In addition, longitudinal incisions are made in the deep fascia of the lower leg at all sites where the presence of incompetent communicating veins has been suggested either by tourniquet test or by phlebogram. Through these incisions the fascia is undermined in the manner described by Linton,[6] thus allowing visualization of the communicating veins

as they pass through the fascia overlying the muscles. It has been observed that many of these communicators do not connect directly with the main saphenous trunks and would consequently be overlooked even on the medial aspect of the leg if only a stripping were performed.

RESULTS

A careful record has been maintained on each patient for comparison of the results of tourniquet test, phlebogram and operative findings respectively.

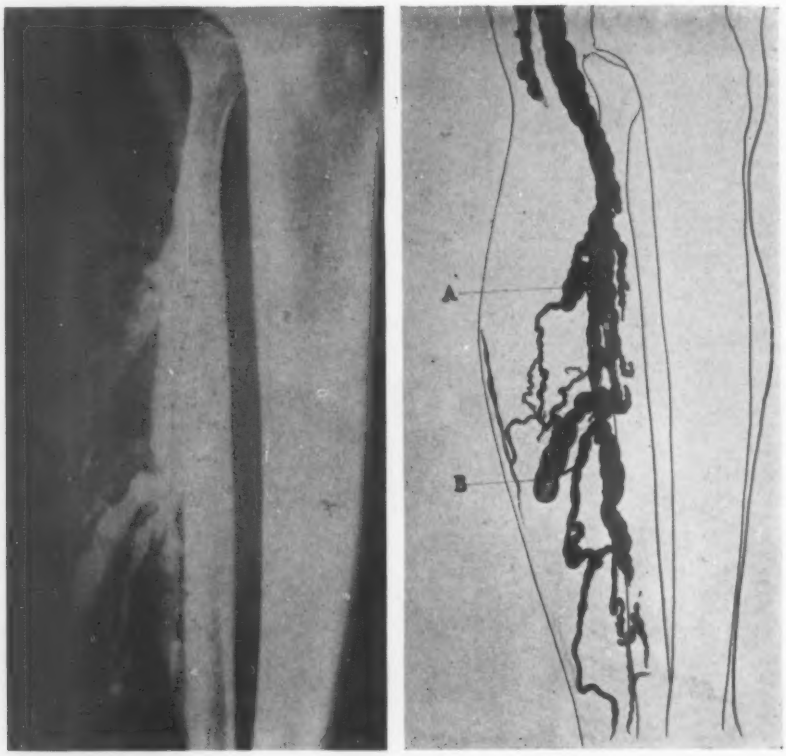

FIG. 3.—Lateral view of lower leg shows two large incompetent perforating veins through which the short saphenous system is filled. It is obvious that high ligation of the short saphenous vein would alone be of little value in this case.

So far twenty patients have been studied. The results are tabulated in Table I and Table II.

Neither the tourniquet examination nor phlebography correlates completely with the operative findings. However, only 54% of the incompetent veins localized by tourniquet preoperatively were confirmed by surgery whereas the results of roentgen-ray localization were confirmed in 86%. Many of the false positives by phlebography represent errors in interpretation of the roentgen-ray findings. These errors have now been largely eliminated with more experience.

TABLE I.

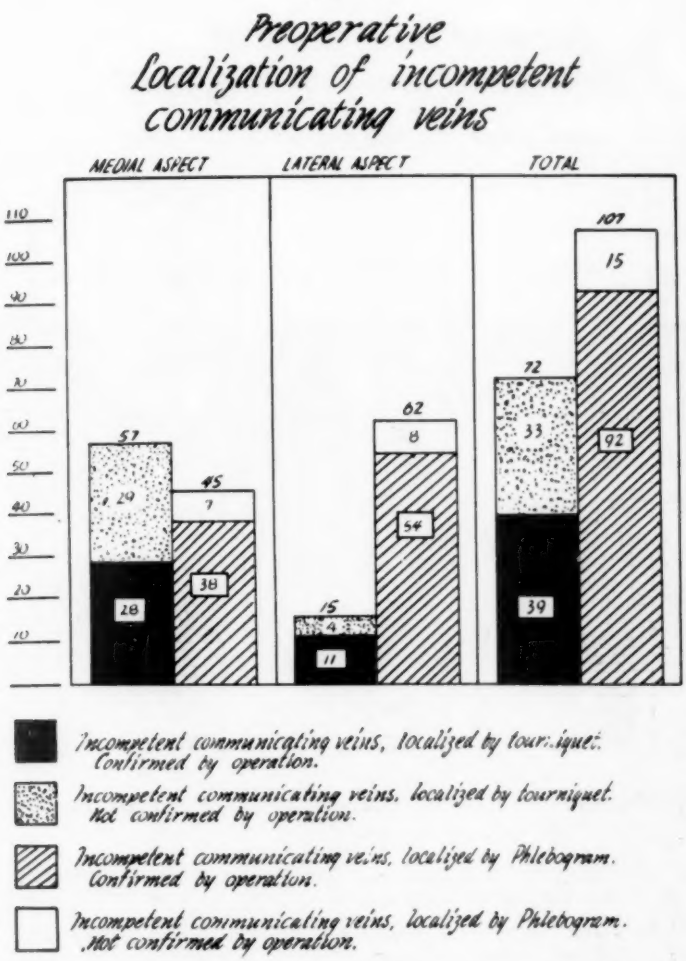

TABLE I.—The numbers of incompetent communicating veins indicated respectively by tourniquet examination and by plebogram are charted side by side. The shaded lower portion of each bar represents the number of incompetent communicators confirmed by operation and the light upper portion represents the number not found by operative exploration. The latter may be termed false positives. The accuracy of phlebography is obviously greater for medial communicating veins as well as over all but the proportion of false positives is about equal on the lateral side of the leg for tourniquet and Roentgenogram.

When the postoperative findings are analyzed it seems that tourniquet examination, with a localization accuracy of only 29%, compares poorly with phlebography, with an accuracy of 69%. Actually the operative findings are themselves not necessarily completely accurate. Probably some communicating veins indicated by clinical or roentgen-ray examination were missed at operation because of inadequate exploration. Furthermore, the decision as

TABLE II.

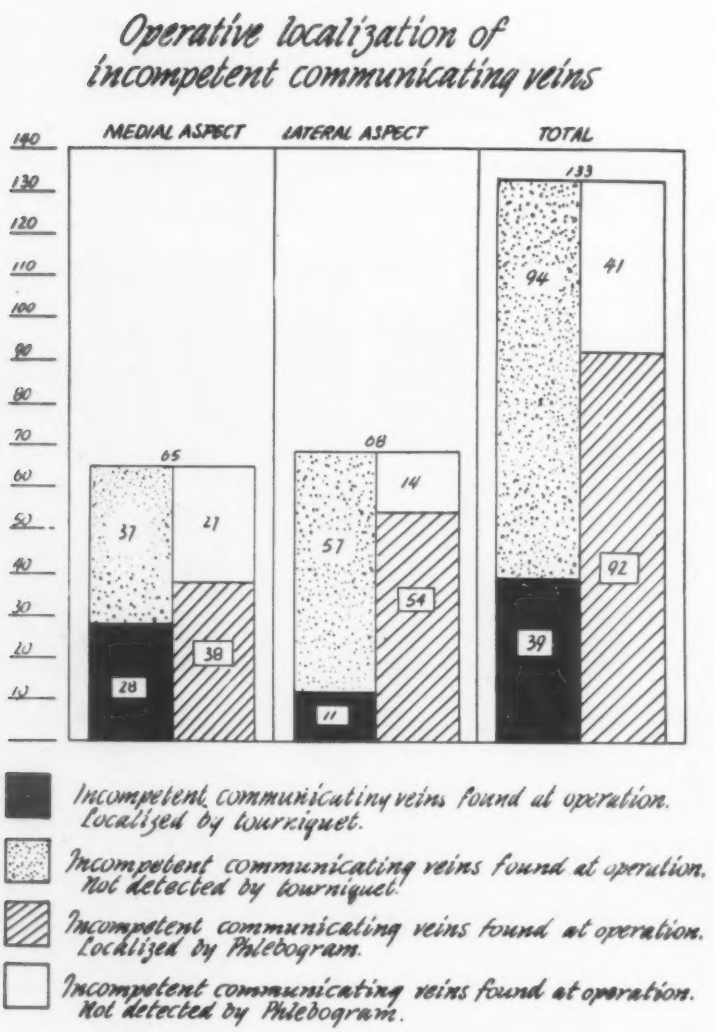

TABLE II.—The number of incompetent communicating veins actually found at operation is indicated. Again the two methods of localization are charted side by side. The dark lower area of each bar represents the incompetent veins which were localized correctly before operation. The lighter upper area indicates the number which were missed pre-operatively. Here the huge difference between tourniquet and phlebogram on the lateral leg is striking.

to competence or incompetence at operation is necessarily based on the size and tortuosity of the communicating veins. Some of those which were classified as incompetent may have been large but nevertheless still competent. In a dissecting room study of the position and size[7] of the lower leg communicating veins, one of us has observed the frequent occurrence in normal

legs of rather large veins connecting the long saphenous with the deep venous system.

DISCUSSION

Clinical examination by tourniquet test or similar methods is necessarily inaccurate for localizing incompetent communicating and perforating veins, especially below the knee, since the segments of superficial vein which become visible between tourniquets are usually not directly over the incompetent communicating veins. This difference between the location of the visible varicosities and that of the incompetent connections through which the former are

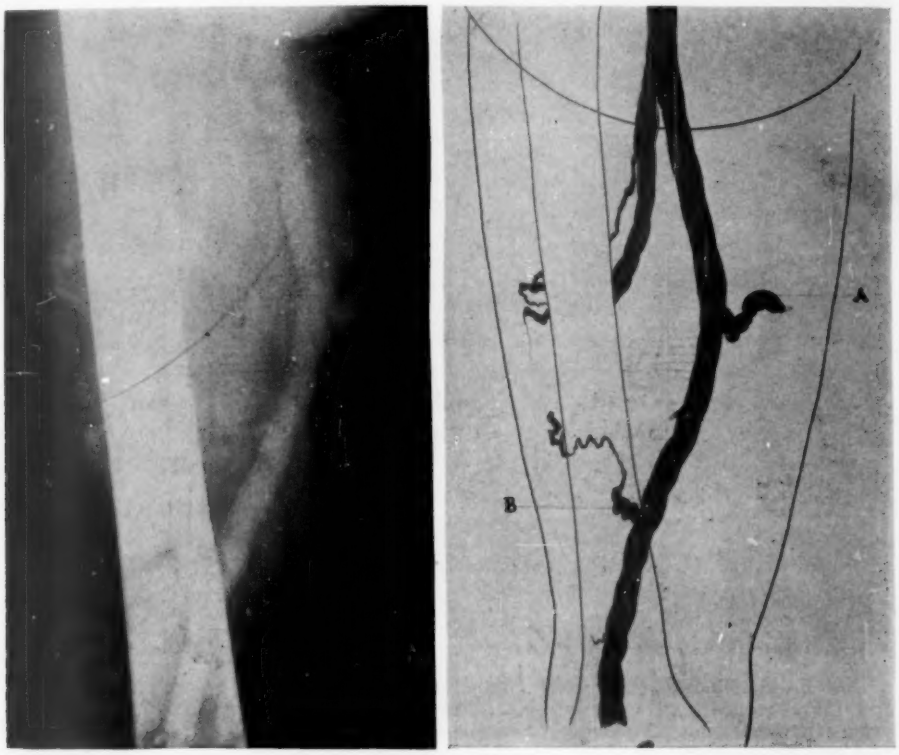

FIG. 4.—Phlebogram of thigh which shows at (A) an incompetent vein corresponding to the mid-Hunter canal perforator of Sherman. The tortuous dilated vein seen at (B) seemed to have no connection with the superficial system which would be demonstrated at operation.

filled is especially manifest when the communicating veins are on the lateral half of the leg. Thus only 16% of the incompetent communicators in this location were detected by tourniquet examination.

The false positives of clinical examination were chiefly on the medial aspect of the leg where over 50% of the incompetent veins indicated prior to operation were not confirmed at surgery. The chief source of error here was probably the effect of pooling of blood in large saccular varices.

The use of phlebography in patients with varicose veins has previously been limited to demonstrating patency of the deep venous system. The rationale of the technic here used is as follows. The tourniquet above the malleoli blocks the superficial venous channels forcing the injected material into the deep veins. As long as the deep channels are free of obstruction the opaque medium does not return to the superficial veins. However, the two

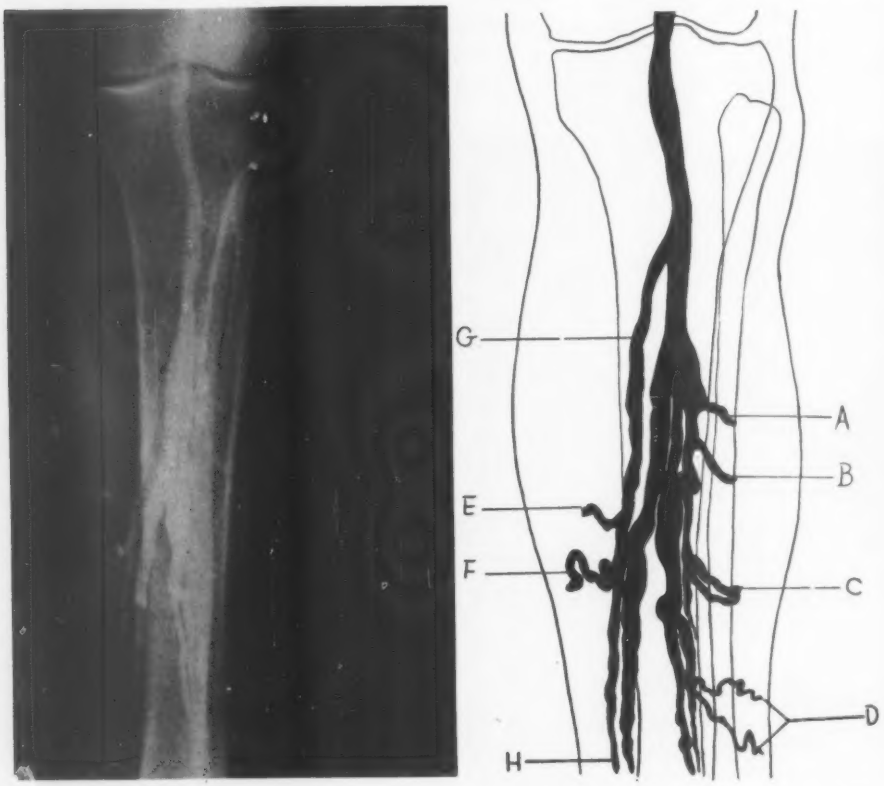

FIG. 5.—Six lateral incompetent communicators are indicated: One each at (A) and (B), two each at (C) and (D). A medial vein is seen at (F). All were proven at operation. Additional communicating veins were found at surgery at (G) and (H), where the posterior tribial veins are not well visualized. On reviewing the plebogram,afteroperation, a faint but definite outline of a communicating vein was observed at (G). There seems to be a medial communicator at (E) but this is an artefact. Actually it is a superficial tributary of the saphenous vein which overlies the posterior tribial veins.

tourniquets on the thigh provide enough obstruction to normal flow to cause the diodrast to pass retrogradely through incompetent communicating veins back to the superficial system. In an extremity with competent valves in the communicating veins, the opaque medium forces its way by the tourniquets instead of through the competent communicating veins.

Thus the visualization of any communicator or perforator by roentgen-ray would depend upon the competency of the valves and be more or less indepen-

dent of the size of the vein. In this respect the phlebogram may be more accurate than the operative findings. On the other hand incompetent communicating veins will be visible by roentgen-ray only when there is good filling of the deep veins with which they are connected. It is difficult to get a good injection of all three pairs of deep veins in the lower legs. The anterior tibials are the most difficult to visualize and at times the posterior tibial veins are not completely filled. Visualization of the peroneal veins is almost always excellent. Recently, by simultaneous injection of two superficial veins on opposite sides of the foot, we have been able to fill all six deep veins in some cases. Non-filling is the basis for most of the missed communicating veins.

With improvements in roentgen-ray technic and interpretation, it is possible that incompetent communicating veins may be localized with sufficient accuracy to justify a new type of operative procedure for varicose veins. This would consist of a high saphenous vein ligation supplemented by local subfascial exploration limited to those sites at which incompetent communicating veins have been demonstrated by phlebography.

SUMMARY

The late results of varicose vein treatment by high saphenous vein ligation are unsatisfactory because of the presence of incompetent communicating veins not detected by tourniquet examination. A phlebographic technic for localizing incompetent communicators is described along with the operative findings in 20 patients. The phlebogram seems to offer a more accurate method than clinical examination for detecting and localizing incompetent communicating veins. Phlebography is particularly useful for mapping lateral communicators which can not otherwise be detected.

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PERFORATION OF ILEUM BY INGESTED CHICKEN BONE COMPLICATING VENTRAL HERNIA*

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THE PURPOSE OF THIS REPORT is to present an unusual case and a discussion of ingested foreign object perforations with special reference to this complication in hernias.

CASE REPORT

Patient A. L., a 51-year-old white male of Czechoslovakian birth, entered St. Luke's Hospital at 7:15 A.M. on April 5, 1945. For the past five years, following an appendectomy through a right rectus incision, he had noted a ventral hernia of increasing size. Seven hours prior to admission, acute cramp-like pains were noted in and around the hernia with marked tenderness of the hernia. He complained of nausea and belching, but had not vomited. A normal bowel movement three hours prior to admittance was reported to have offered no relief from the pain. The past history, except for appendectomy and subsequent hernia, was negative.

Examination revealed an obese white male, anxious and obviously in pain. BP—125/90; Temp.—100.2 (oral); Pulse—132; Resp.—32. Complete upper and lower artificial dentures were present. Neck, heart and lungs were normal. A grapefruit-sized ventral hernia protruded from the right para-umbilical region. It was tender, hot and irreducible. Bowel sounds were not present within the hernia, and were heard but occasionally in the adjacent abdomen. Laboratory: RBC—4,600,000; WBC—10,650; Hgb.—14.6 Gm.; urine-chemical and microscopic, negative.

A diagnosis of strangulated ventral hernia was made, and immediate operation advised.

Operation was carried out under ethylene-nitrous oxide anesthesia supplemented with curare intravenously as needed for additional relaxation. The old lower right rectus skin scar was excised. The hernial sac was dissected out and opened. It contained several loops of ileum, three of which were markedly hyperemic and covered with fibrinous exudate. Remaining loops were only slightly cyanotic. Purulent exudate with a foul odor was present in the sac. Two loops of ileum deep in the inferior portion of the sac were found to be adherent to the peritoneum lining the sac. Both fibrous and fibrinous cohesion was encountered. In the course of freeing one of the loops, a chicken bone fragment was discovered protruding through a necrotic patch on the antimesenteric margin of the ileum. The bone was extracted after enlarging the perforation. The serosal fat tags were cleaned from the surrounding ileal surface and purse string closure made. As none of the involved intestine presented permanent circulatory embarrassment,

* The assistance of Miss Angeline McNeil, St. Luke's Library, is gratefully acknowledged.

all loops were reduced into the abdominal cavity. The excess sac was trimmed away and a layer closure of the defect was carried out. Single 0 chromic catgut was used to imbricate the peritoneum and posterior rectus sheath, and interrupted #20 cotton sutures were used in the anterior rectus fascia. Sulfanilamide crystals were dusted between the layers.

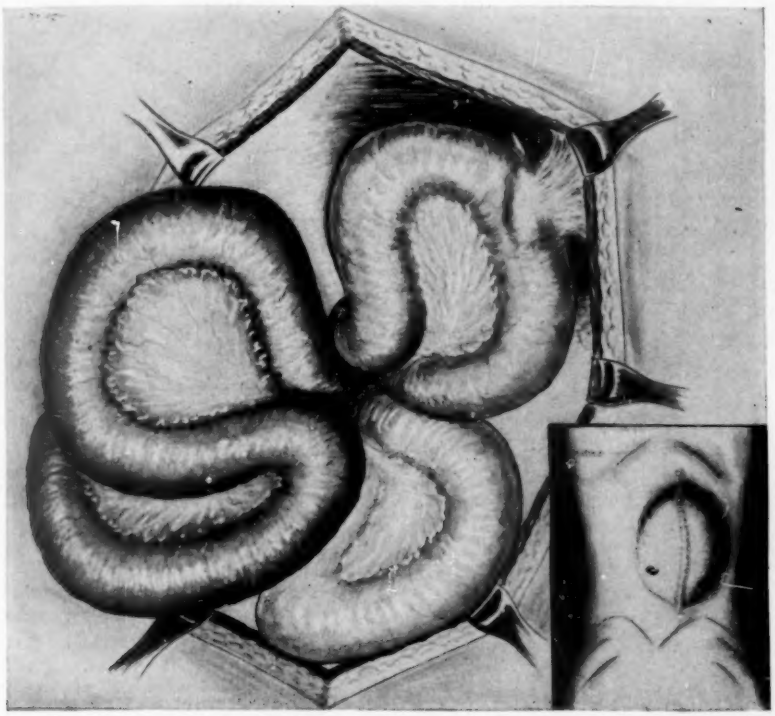

FIG. 1.—A sketch of the opened sac of the ventral hernia showing adherent ileum which has been perforated by chicken bone (lower left). Inset represents site and size of hernia.

TABLE I.—*Age and Sex of Patients Presenting Foreign Body Perforations in Hernias.*

Adults	31	Males	19
Children	7	Females	14

TABLE II.—*Types of Hernia in Which Foreign Bodies Have Been Found.*

Inguinal	24	Umbilical	5
Femoral	4	Incisional	2
		Epigastric	1

The patient withstood the procedure well. A severe test of the closure was encountered when the patient underwent a reaction of marked excitement during recovery from the anesthetic. Supportive intravenous fluids, vitamins B and C, and sodium sulfadiazine were given for four days after which the patient resumed oral feedings. Oral sulfadiazine

was continued for eight days. The maximum temperature of 101.2 was reached on the third postoperative day. A moderate amount of induration appeared late in the lower angle of the wound, was followed by serous drainage for a few days, then complete healing. The patient was discharged, well, after seventeen days of hospitalization. When last seen six months following operation, his wound was firmly healed and his general condition good.

History obtained subsequent to operation included his recollection of inadvertently swallowing the chicken bone about two weeks prior to the acute episode.

DISCUSSION

The ingestion of foreign objects is undoubtedly quite a common occurrence. Perforations of the gastro-intestinal tract resulting from this are fortunately much less common. In a group of 800 patients with foreign bodies in the gastro-intestinal tract observed at Boston City Hospital, Henderson and

TABLE III.—*Description of Ingested Foreign Objects Causing Intestinal Perforations in Hernias.*

Bones, total	21	One instance each	
Chicken	9	Wire	
Hog	3	Nail	
Fish	3	½ set false teeth	
Frog	1	Earthen egg cup	
Lamb	1	Claw of skylark	
Fruit seeds	6	Head of barley	
Needles	5	Lead pencil	
Pins	2		

TABLE IV.—*Treatment and Mortality*

	No. of Cases	Mortality
Unoperated	6	50%
Incision and drainage (including enterostomy)	6	33⅓%
Hernioenterotomy	25	30% (Based on 17 cases)
Herniotomy and intestinal resection	5	20%
Herniotomy and appendectomy	3	0%
Total operated	37	28% (Based on 28 cases)

Gaston reported only nine perforations, with two deaths. Carp reported 43 cases of which 31 were followed; 25 were uncomplicated, 6 perforated, and 2 died. Macmanus was able to find in the literature 93 reports of perforations, noting that many cases were probably not reported, and that his review was probably not complete. An analysis of this material interestingly discloses that no part of the gastro-intestinal tract escapes perforation and that no definite conclusion can be made regarding the segment of gut most prone to perforation. However, one does note frequently that the pyloric sphincter, duodenal kinks, Meckel's diverticulum, appendix, and small bowel in a confining hernia are the sites involved. Mechanically, this is not unexpected.

The perforating agents most frequently encountered are pins, wires, bones from animal, fowl or fish, and wooden splinters. Teeth, and numerous strange pointed objects are also reported.

In adults, false dentures with concomitant alteration of buccal and pharyngeal sensitivity, apparently predispose to accidental swallowing of the objects.

The reaction which accompanies a perforation varies, depending upon anatomical factors or chronicity. Ginsberg and Beller have presented the following classification:

1. Acute perforation with peritonitis,
2. Localized intra-abdominal abscess,
3. Intra-abdominal inflammatory tumor,
4. Abdominal wall inflammatory tumor,
5. Abdominal wall abscess, and
6. Perforation with inflammation and obstruction in hernia.

The symptomatology and physical findings are usually consistent with the degree of pathology.

The history of swallowing a foreign object coupled with Roentgen-ray confirmation should offer the best chance for establishing the etiology and diagnosis prior to operation. Treatment should be suited to the type of complication encountered in accordance with accepted surgical principles.

FIG. 2.—Photograph of chicken bone removed from adherent ileum in ventral hernia operation.

With our interest directed to *foreign object perforation complicating hernia,* we have made a careful search for case reports and references to this entity. Some of the material was not accessible in original articles, which accounts for lack of complete detail in the analysis to follow. The earliest case was reported by Claudius in 1735. Fabian reviewed 35 cases in 1910, including one in which the foreign body was a gallstone and one an intestinal stone. Our study is based upon the 50 cases thus collected, and includes only perforations by ingested foreign objects.

The incidence with respect to age and sex is shown in Table I. The type of hernia involved is indicated in Table II. Of particular interest is Table III in in which are listed the corpora alieni. The diligence expended upon proper identification of these articles is remarkable.

Variations in treatment with the associated mortalities are shown in Table IV. As one would expect, the highest death rate occurs in cases unoperated, and in those coming for treatment too late for any intervention except incision and drainage. Hernioenterotomy, which entails the extraction of the foreign body, closure of the gut, and repair of the hernia, shows a somewhat better rate at 30 per cent. In the group requiring intestinal resections, the mortality is lowest, *i.e.,* 20 per cent. This number of cases is too few to weigh properly against the previous group. Perforations of the appendix, treated by appendectomy and herniotomy, occurred three times with no deaths. The mor-

tality based on the 28 operated cases, in which outcome was indicated, was 28 per cent.

It was of interest to find in one report only a correct preoperative diagnosis. In this case, the patient offered the suggestion that his trouble might be due to a nail accidentally swallowed some time before. A roentgen-ray study confirmed the suspicion, and the nail was recovered from the appendix at operation.

Ackerman points out the essential differences in mechanics between this entity and primary hernia incarceration. The foreign object lodges and penetrates when it encounters a turn too sharp to allow it to proceed. There follows a variable amount of soiling of the hernia sac, then rapid agglutination of the bowel serosa to the neck of the sac, thus resulting in localized peritonitis. The bowel may not obstruct as rapidly in these cases as in primary incarcerations caused by a tight ring. It is therefore not uncommon that obstructive symptoms are delayed out of proportion to the local physical findings of a strangulated hernia. As the local peritonitis increases, however, one may expect an intensification of obstructive and general symptoms.

The ideal treatment should consist of relieving the bowel of the perforating object, closure of the bowel, (or resection and primary anastomosis if necessary) and repair of the hernia. Compromise procedures may be indicated, limiting one to drainage of the abscess, and decompression of the obstructed bowel. The resulting enterostomy or fistula will then require such secondary closure as is needed when the general condition of the patient permits.

The lowering of mortality in this group will parallel that of other abdominal emergencies in which early recognition by the patient and early operation exert such a favorable role on the outcome.

SUMMARY

A case history is presented in which the patient, operated for a strangulated ventral hernia, was found to have a chicken bone perforation of the ileum with inflammation and obstruction of the bowel loops contained in the hernia. Recovery followed the removal of the chicken bone, closure of the ileum and repair of the hernia.

Considering the number of foreign bodies swallowed, the incidence of reported complications is very low. Such complications as have resulted include perforation and obstruction in hernias, of which 50 cases have been collected from the literature and analyzed. Bones outnumber other objects. Inguinal hernias are involved more often than other types. There were 11 deaths in the group of 36 cases for which this information was available.

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THE ACCIDENTAL OPERATIVE TRANSPLANTATION OF BENIGN GIANT CELL TUMOR

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THE NATURE OF GIANT CELL TUMOR of bone has been frequently discussed in the past few decades. In recent years it is more generally believed to be a type of benign bone tumor which may have local destructive powers with the ability to recur at the primary site and yet does not give rise to distant metastases. Meyerding[5] has suggested the use of the terms "benign giant cell tumor" and "malignant giant cell sarcoma" to differentiate the more common type from the malignant tumor.

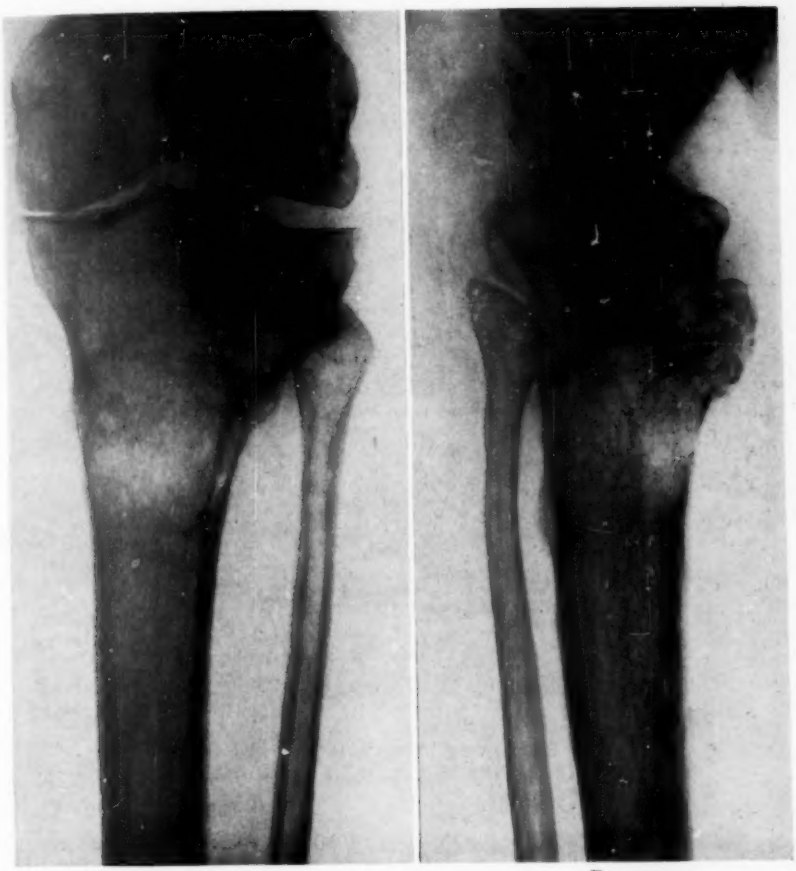
The possibility of metatases arising from benign cell tumor, however, has been thoroughly reviewed in the literature. It has been indicated that pulmonary metastases might be expected from this benign tumor in view of its free vascular connections and the frequent treatment by curettage. Ewing made a careful search for such cases up to 1926 and pointed out that in spite of numerous efforts, no proven cases of metastases from benign giant cell tumor had been reported. Meyerding[6] in his large series of 40 cases treated by excision of the tumor and bone graft had no instance in which there had been a transplantation of a benign giant cell tumor.

This case report concerns the accidental operative transplantation of a benign giant cell tumor of the tibia to a distant soft tissue site over the crest of the ilium. No similar case was encountered in the literature.

J. M., a 56-year-old railroad worker was admitted to Toronto General Hospital on April 11th, 1946, with a history of intermittent swelling below the left knee for 5 months associated with slight pain and stiffness in the knee for 2 months. Five weeks before admission about 50 cc. of straw colored fluid had been aspirated from the knee joint with some relief of symptoms but one week previous to admission the patient developed an acute thrombophlebitis of the left leg. On admission the left knee presented a hard diffuse slightly tender swelling in the upper end of the tibia and roentgen-ray showed an expanding osteolytic lesion of the upper end of the tibia which had broken through the cortex at the level of the tibial tubercle, (Fig. 1). A biopsy of the tumor showed a typical histologic picture of benign giant cell tumor, with varying numbers of large irregular giant cells scattered throughout a fibrous tissue stroma. These giant cells had numerous hyperchromatic nuclei which were located usually in the central portion of the cell. (Fig 2).

On May 8th, 1946, the tumor mass was curetted leaving a large cavity in the upper end of the tibia about four inches in length. The defect was bridged with a sliding bone graft from the tibia and the remainder of the cavity was packed with cancellous bone chips obtained from both iliac crests. The can-

cellous bone graft was removed *after* the curetting of the tumor. Figure 3 shows an immediate postoperative roentgenogram with the limb in a circular plaster. The cast was removed and reapplied after two months with no evidence of recurrence of the tumor. On October 5th, 1946, five months postoperatively the patient was readmitted and on removal of the plaster cast a moderate sized swelling of the upper end of the tibia was noted. Roentgenogram showed



A B

FIG. 1 (A).—A.P. X-rays to show the expanding osteolytic lesion of the upper end of the tibia—broken through at the level of the tibial tubercle. (B)—Same as on Fig. 1 (A).

a local recurrence of the tumor involving the whole upper end of the tibia. On October 16th, 1946, the upper end of the tibia and the tumor were excised and a massive tibial graft from the right leg was used to bridge the gap from the lower end of the femur to the middle of the left tibia. Cancellous bone chips from the upper end of the right tibia were packed about the graft. The microscopic sections of this tumor showed a recurrent giant cell tumor of bone with numerous variable sized multinucleated giant cells distributed through in-

terbranching bundles of fusiform fibroblastic cell elements. Additional sections of adjacent skeletal muscle tissue did not show any evidence of invasion of the tumor growth, (Fig. 4). The limb was immobilized with external skeletal fixation but slight infection developed about the upper two Rodger-Anderson pins. As a result the Rodger-Anderson apparatus was removed and a plaster spica applied (Fig. 5). Unfortunately the patient developed a mild infection in the wound at the left knee and a window was cut in the cast in the area of the sinus.

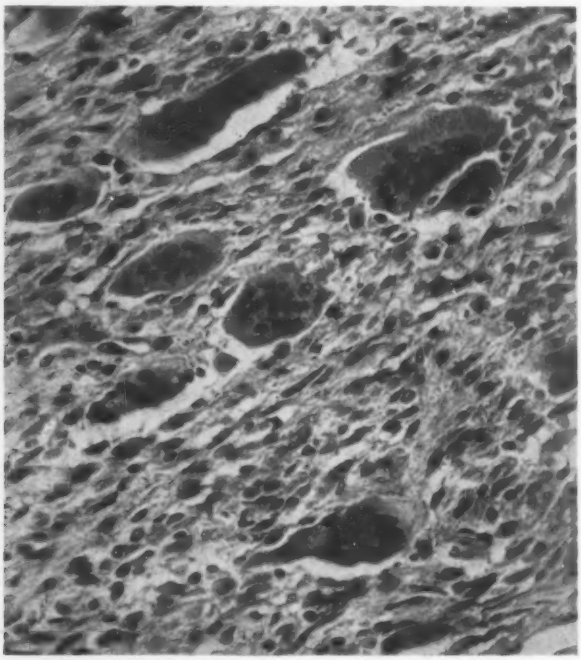
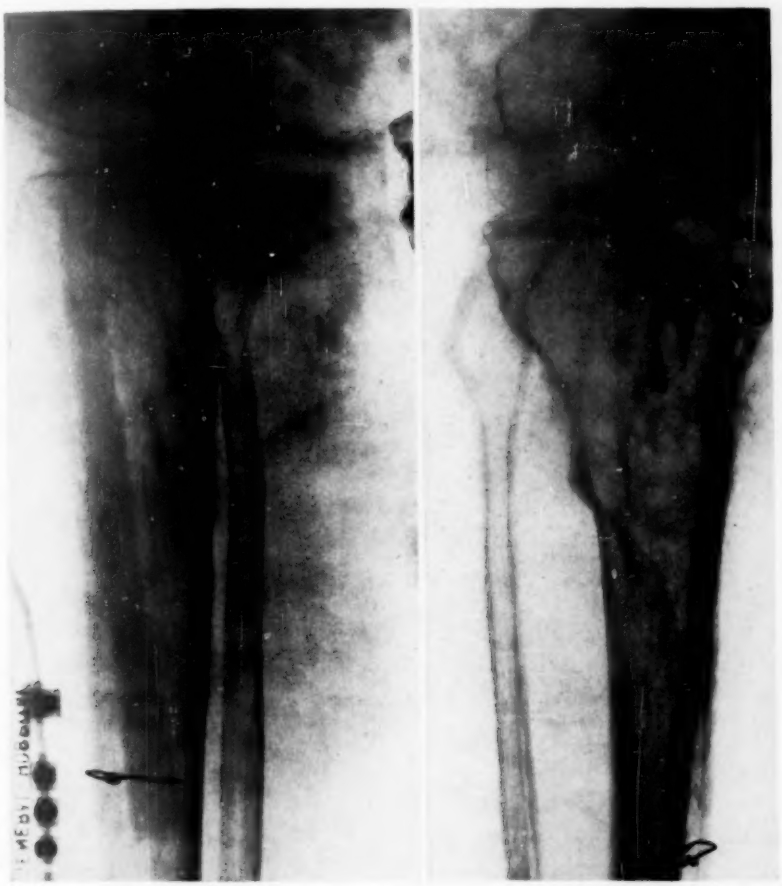


FIG. 2.—Biopsy from tumor of the upper end of the tibia showing varying numbers of irregular giant *cells* scattered throughout a fibrous tissue stroma.
circular plaster.

On February 22nd, the plaster spica was removed and at this time a firm mass about 1½" in diameter was noted beneath the scar over the left iliac crest at the site of previous cancellous bone graft (May 8th, 1946). A biopsy of this mass was taken and on March 5th, 1947, the tumor was widely excised. Figure 6 shows the gross specimen, bisected. It was situated superficially beneath the skin and was attached to scar tissue overlying the ilium. There was no attachment to bone. This implantation tumor revealed the characteristic picture of benign giant cell tumor of bone in the gross. The histologic appearance was similar to the sections previously described. In addition there were a few areas of patchy necrosis and haemorrhage (Fig. 7). Careful physical examination failed to reveal any further masses and roentgenograms of the pelvis and chest were negative.

DISCUSSION

Experimentally the innoculation and implantation of malignant tumor cells have been successfully carried out under certain conditions. This has been demonstrated well by transplanting sarcoma and carcinoma in rats and mice. Ewing, in discussing the essential conditions for neoplastic growth of misplaced cells, state that the cells must possess some special capacity for



A B

FIG. 3.—X-ray immediately postoperative (May, 1946) with limb in

growth, either by virtue of an embryonal character or from retention of proliferative tendencies in more than ordinary degree.

Clinically, operative transplantation of carcinoma has been frequently reported in the literature. Corniel in 1891[3] reported successful tumor transplantations from a malignant tumor of one breast to the other breast. Ryall, in 1907,[9] pointed out that recurrent carcinoma was frequently due to contamination of the instruments with cancer cells. Ryall was the first to advocate a complete change of gloves, drapes and instruments followed by re-

preparation of the operative site after a biopsy of a malignant tumor. Primrose in 1922[3] briefly recorded a case of an ovarian malignancy in which ascitic fluid was aspirated and subsequently injected in the submamary region as an experimental therapeutic procedure; a malignant tumor appeared in the breast and axillary glands.

The demonstration of viable tumor cells on instruments used for biopsy of a carcinoma of the breast was made by Saphir.[10] Smears were made directly

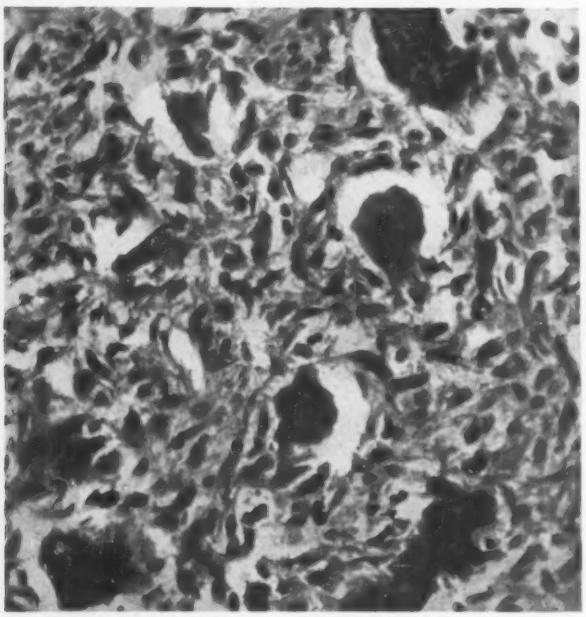


FIG. 4.—Biopsy from recurrence of tumor showing numerous variable sized multinucleated giant cells distributed through bundles of fusiform fibroblastic cell elements.

from knife blades and from saline in which such blades had been rinsed. Brandes White and Sutton[1] repeated this work and also demonstrated viable malignant tumor cells in basins of water in which the surgeon's gloves were washed. The cells appeared to remain viable for longer periods in saline than in distilled water. They reported a case in which it seemed evident that contamination of the gloves was responsible for transplantation of highly malignant carcinoma of the breast from the mastectomy site to a skin donor area on the left thigh.

The implantation of benign tumor cells, however, appears to be uncommon. Sampson studied the occurrence of endometriomata in extra genital positions and this led to his theory of endometrial transplantations. Previous to this time Iwanoff (1889) and others postulated a serosal origin for peritoneal endometriomata. MacLeod in his Hunterian lecture stated that invasion of

endometriomata has occurred along intertissue spaces and he favoured a theory of lymphatic permeation. Sampson's theory, however, still remains the most popular.

Burke[2] has recently reported a case of recurrent parathyroid adenoma occurring in a glandular graft. In 1943 a parathyroid adenoma was completely excised and at operation a small fragment of the adenoma was transplanted

FIG. 5.—X-ray to show limb following treatment to recurrence after Rodger Anderson pins removed and limb encased in plaster.

between the sternothyroid and sternohyoid muscles in an endeavour to avoid a hypoparathyroid state postoperatively. Two years later the patient had a recurrence of hyperparathyroid symptoms and a benign parathyroid adenoma was removed from the sternothyroid muscle at the site of the graft. In this case a small glandular fragment was intentionally implanted, whereas in the above case report it is indicated that the benign tumor cells were transferred by the instruments or gloves of the operator.

FIG. 6.—Gross specimen from left iliac crest showing implantation tumor. It has been bisected to show the two halves of the implant occupying the lower half of the picture.

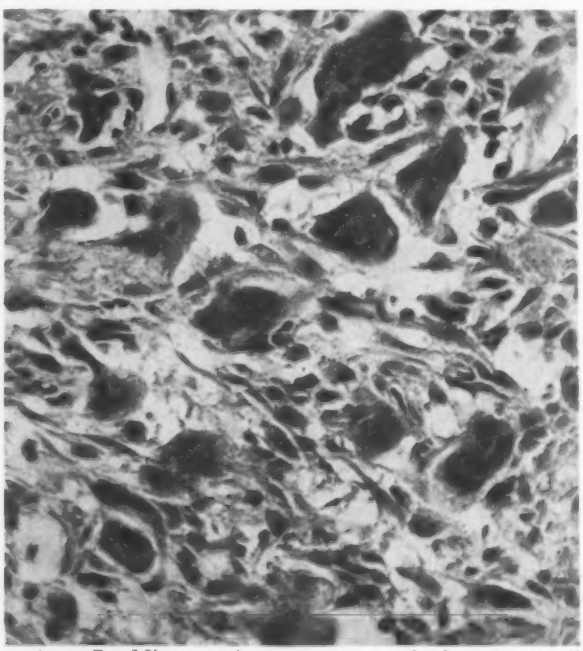


FIG. 7.—Microscopic appearance of the giant cell tumor implant fhich shows the same features as noted in the primary and the local recurrence.

SUMMARY

This case is reported to illustrate the operative transplantation of benign giant cell tumor of bone to a distant soft tissue site.

The primary tumor originating in the upper end of the tibia and the local recurrence 9 months later showed a typical benign histological picture.

The transplantation occurred in the soft tissue in the left iliac region at the site of previous operative interference and it revealed an identical histological picture.

The authors wish to express their thanks to Dr. R. I. Harris and Prof. Wm. Boyd for advice and critcism in the preparation of this paper.

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PRIMARY CARCINOMA OF THE LIVER: REPORT OF A CASE TREATED BY LOBECTOMY*

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THE LOW INCIDENCE of primary malignant tumors of the liver, the presumed difficulty of early diagnosis, as well as the hopeless prognosis usually accorded them, result in a paucity of patients receiving surgical therapy.[1] Although a considerable number of surgical extirpations of tumor of the liver have been reported and summarized (Warvi)[2], the resection of primary carcinoma of the liver remains a relatively rare procedure, and lobectomy is even more uncommon.[3] At the Tumor Clinic, V.A. Hospital, Hines, Illinois, from 1934 to 1946, 36 cases of primary liver cell tumors were authenticated either at operation or post mortem examination. Of these only one was resected.

CASE REPORT

J.D.K., a 49 year old white cook of Greek origin, entered the V.A. Hospital, Hines, Illinois, July 7, 1942, complaining of a mass in the upper abdomen. Save for a brother who had echinococcus disease of the liver, the family history was not significant. The patient had travelled considerably but had arrived in the United States at the age of 17 and remained within its continental borders. In Army service (1917-1919) diagnosis of minimal pulmonary tuberculosis and chronic pleurisy were established, but the patient had had no symptoms referable to the chest for the past twenty years. The use of alcohol was limited during the past 34 years to a few glasses of dry *unrosined* wine daily.

Approximately one year before his admission, the patient complained of gaseous distention after meals which was reliefed by alkaline powders and restriction of fats in his diet. In January 1942 he noted a small pea-sized nodule high in the epigastrium, which remained in the midline when the patient was recumbent and shifted to the left when erect. Just prior to his admission, he had two severe attacks of epigastric pain. These occurred about two hours after meals and lasted 15 to 20 minutes, when they were relieved by the use of alkaline powders and a heat pad. The patient stated that his weight had remained stationary for the past 10 years. There was no history of nausea, vomiting or melena, and a systematic review of symptoms revealed no abnormalities. The constant slow growth of the nontender lump in the abdomen had caused him to seek hospitalization, but he stoutly maintained that he did not feel sick.

Examination showed a slight, poorly nourished, white male of 65 inches, weighing 107 pounds. The abdomen was slightly scaphoid, soft, and nontender. No scars or unusual surface veins were evident. In the left upper quadrant there was a nontender, ballotable, round mass approximately 7 cm. in diameter, which moved readily with respiration and showed no connection with the abdominal wall. Neither the liver edge nor the spleen could be felt.

Roentgen-ray study of the chest revealed an old, healed, calcified focus in the right subapical region, as well as pleural calcification at the right base. A gastro-intestinal

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study disclosed no evidence of esophageal varices, but did show an extrinsic pressure defect of the greater curvature of the stomach with a secondary pressure defect of the greater curvature of the pylorus. There were no intrinsic gastric defects, but the duodenal cap showed slight irregularity of the left anterior border. Barium study of the colon revealed no abnormalities. Electrocardiogram showed a slurred QRS_3, a low T, and a decreased ST_1, ST_2. Fractional analysis of gastric contents showed a free acid varying from 0 to 8 and total acid from 16 to 26, with a trace of occult blood. No parasites were found in three examinations of the stool, with only a faint trace of blood in one specimen. Urinalyses were negative. Red blood cells averaged 4,300,000 per cu. mm. with 85% hemoglobin and leukocytes varied between 12,000 and 10,000 per cu. mm. with a differential count averaging 50 polymorphonuclear cells, 48 lymphocytes, and 2 eosinophiles. Wasserman and Kahn tests were negative. Blood chlorides were 544 mg. per 100 cu. cm. Urea nitrogen 15.4 mg. per 100 cu. cm. and sugar 76.9 mg. per 100 cu cm. Icterus index varied from 9 to 12. Prothrombin time (Quick) was 100%. Tubercle baccili were not found in any of the five sputum specimens.

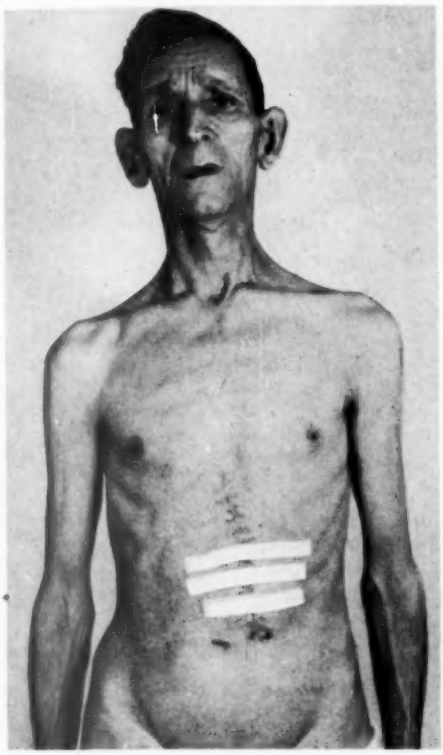


FIG. 1.—Photograph of the patient just prior to discharge. Preoperatively a mass was palpable in the left upper quadrant of the abdomen but could not be shown by a photograph.

A preoperative diagnosis of a hepatoma, left lobe of liver, or pancreatic cyst, was made and, on August 20, 1942, under gas-oxygen-ether anesthesia, operation was performed through a left upper paramedian incision. Careful examination was made of the entire peritoneal cavity and, with the exception of the liver, findings were normal. The liver showed a fine nodularity and was somewhat firmer than normal. A round, yellow-green, soft, partially cystic tumor, 6 cm. in diameter, was noted in the left lobe of the liver. The tumor was elevated approximately 1.5 cm. above the plane of the anterior surface. Upon aspiration, a small amount of necrotic debris was obtained. Immediate microscopic study by the pathologist showed cells indicative of hepatoma. No other lesions were found and the decision was made to resect the left lobe of the liver.

The liver substance was suture-ligated with enveloping sutures along the umbilical incisure and the falciform ligament with No. 0 chromic catgut on a long needle. Due to the cirrhosis of the liver, it was firmer than normal and retained the sutures well. The phrenic ligament was sectioned and the left lobe of the liver severed with the scalpel just to the left of the sutures. The raw surfaces were partly approximated with interrupted mattress sutures. A free omental graft was then obtained and fastened over the resected end of the liver with No. 00 catgut sutures. No bleeding was noted and the abdominal wall was sutured in layers. 500 c.c. of whole blood and 1,000 c.c. of 5% glucose were given intravenously during the operation. The patient's condition was excellent throughout the entire procedure.

Pathologic report by Dr. William McNamara was as follows: "Specimen is the left lobe of the liver, which measures approximately 15x8x6 cm., containing an encapsulated tumor mass in the central portion which measures 5 cm. in diameter. The mass on cross section is lobulated and has a grayish-greenish color; it shows some evidence of degeneration. The liver proper is hobnail in type. Microsection of tumor discloses cords of cells which resemble the liver cords quite closely. The nuclei, however, are quite hyperchromatic and show some variations in size. The cytoplasm for the most part is granular to fairly clear. There is some variation in size of the cells and an occasional mitotic figure is noted. Many of the columns of cells are surrounded by a blood space. There is very little or practically no fibrous stoma. The lesion is quite typically of a liver cell origin and imitates the liver quite closely. Microsection of the liver also discloses an early portal cirrhosis

FIG. 2.—Section through the anterior surface of the left lobe of the liver and directly through the tumor. Note the nodularity of the surface of the liver.

with some increase in connective tissue and quite an extensive round cell infiltration throughout the portal areas. There is some reduplication of the bile ducts. The liver cells proper are divided into lobules by the connective tissue and show some evidence of hyperplasia. All the cells are mildly granular.

DIAGNOSES: Solitary hepatoma, liver
Cirrhosis, portal, early."

Convalescence was slow but uneventful. Blood chemistry postoperatively showed a normal urea nitrogen of 14 mg. per 100 cc.; cholesterol of 200 mg. per 100 cu. cm.; albumin 3.9 Gm.; and globulin 2.4 Gm., with a total protein of 6.3 Gm. per 100 cu. cm. Takata-Ara test showed a strong positive reaction. The patient was discharged on September 28th, symptom-free.

Follow up in April 1943 revealed that, while the patient had gained ten pounds in weight, he tired easily and had occasional pains in the left upper abdomen. Examination revealed a postoperative hernia in the abdominal scar, which was well controlled by means of an elastic support. No abdominal masses were palpable. In October of the same year, the patient reported a dull left upper quadrant ache. He was seen again in

April 1944, but his condition remained unchanged. Between the time of this follow up and his final admission, July 6th, the patient developed edema of both lower extremities, an increase in girth of the abdomen, a dragging sensation in the lower abdomen, infrequent but fairly sharp left upper abdominal pain, progressive enlargement of the hernial protrusion, as well as weight loss, weakness and yellowing of the skin.

Examination revealed a chronically ill, frankly icteric, weak, poorly nourished male, in no acute distress. His height was 5 feet 5 inches, his weight 115 pounds. Blood pressure was 95/60. The pertinent physical findings were limited to the abdomen. The large upper left pararectus incision was well healed, but there was a diastasis of the underlying rectus musculature. A large, firm, freely movable, midepigastric and right upper quadrant mass was palpable, presumably liver, which could be freely ballotted within the abdominal cavity. There was also present a moderate amount of ascites. The patient's icterus index varied from 30 to 60; his cephalin flocculation test was reported as plus 3; his van den Bergh revealed a delayed direct reaction; urine was reported as dark amber, with a specific gravity of 1,024, showing no formed or cellular elements. The serum protein was reported as 6.3 mg. per 100 cu. cm.; albumin, 3.4 Gram. per 100 cu. cm.; and globulin, 2.9 Gm. per 100 cu. cm. Blood cholesterol was reported as 225 with 60% esters. Bromsulfalein test showed 80% retention for one half hour and 70% for one hour. Stools showed stercobilin and no evidence of occult blood. Despite supportive therapy, the patient developed progressive abdominal distention and ascites and retrogressed steadily. He died July 29, 1944, 23 months after lobectomy.

At autopsy no evidence of extrahepatic metastases was found. Both lungs were waterlogged; spleen showed congestion; kidneys were edematous and the adrenals showed some cortical atrophy. Dr. McNamara's findings in the abdomen and liver follow:

> "In the anterior abdominal wall . . . . there was practically no subcutaneous fat with a separation of the muscles and fascia in the upper abdomen and herniation under the skin. About 2500 c.c. of green fluid was found in the peritoneal sac. Left side of the liver was covered by dense adhesions where the left lobe of the liver was resected and the stomach was adherent to the area. No lymph gland enlargement was found. The liver weighed 1700 Gm., was green and nodular, and showed hobnail cirrhosis. In the liver substance there were four large nodules, softer than the remainder of the liver, circumscribed by connective tissue, gray-brown with a greenish cast. The largest measured 6 cm. in diameter. These were hepatomas similar in appearance to the large hepatoma of the left lobe of the liver which was resected surgically. The left end of the liver from which the left lobe was removed was covered with scar and there was no evidence of recurrence at this site. The esophagus and stomach showed many large dilated veins in the walls but no evidence of rupture."

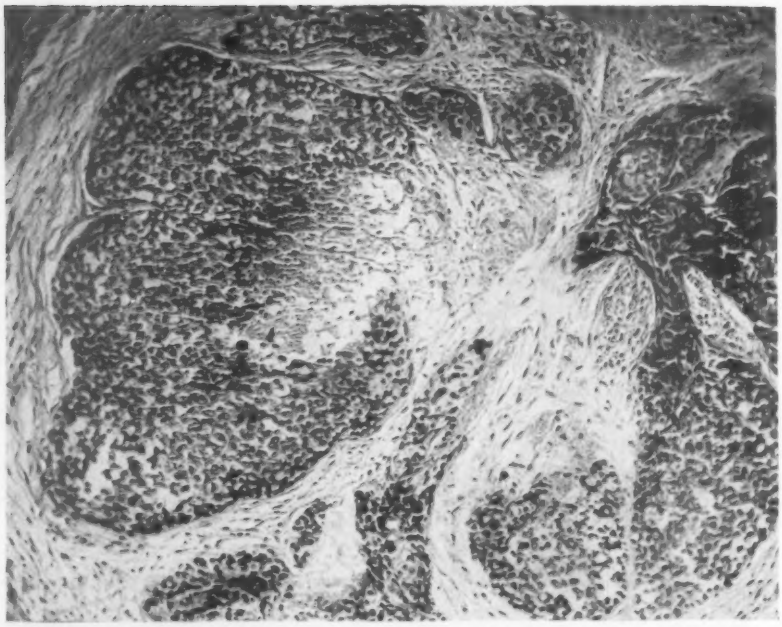
The histopathology of the tumor was unchanged from the previous report.

Although there was no gross evidence of metastasis in the right lobe at the time of operation, it is our belief that microscopic deposits were present. This has been exemplified in two recent personal cases with lesions apparently located in the left lobe. Biopsies of apparently grossly normal tissue showed microscopic evidences of carcinomatous infiltration. It is, nevertheless, possible that in this case the later growths were separate tumors of multicentric origin in a cirrhotic liver.

DISCUSSION

Biopsy is imperative in the diagnosis of liver tumors, and this is best performed during the course of exploratory laparotomy. In concurrence with the opinion of the majority of observers, we have noted but a very few temporary arrests following the present day methods of irradiation of liver tumors, and have been impressed by the many severe and harmful reactions.[4, 5] Although peritoneoscopy with biopsy has been advocated, it is our opinion that an exploratory laparotomy adds but slightly more trauma to the properly prepared patient, and aids greatly in the decision of resectability. Every case

FIG. 3



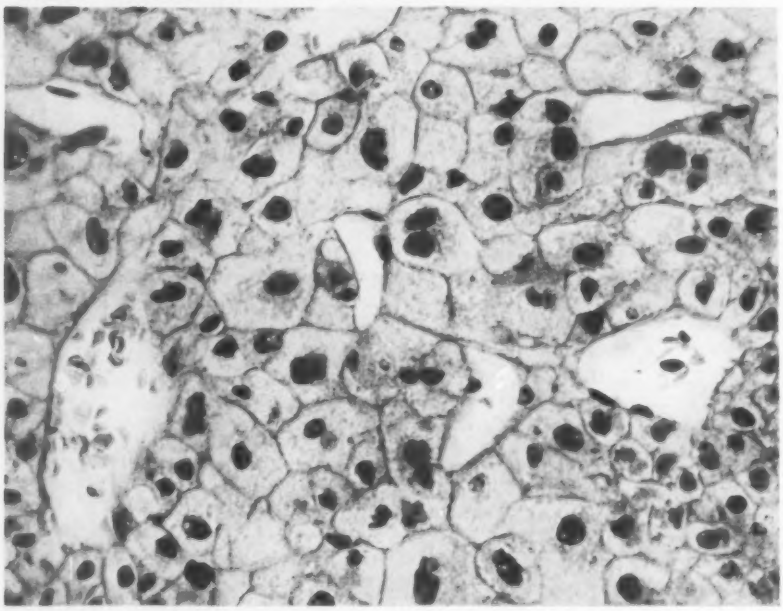


FIG. 4

FIG. 3.—Low power photomicrograph (100x) of tumor showing expansive growth in all directions, central necrosis and fibrous stroma. Note nuclear variability.

FIG. 4.—High power photomicrograph (450x) of field of Fig. 3, showing irregular nuclear outlines, hyperchromatism, and mitotic figures. Note resemblance to liver cells and relation to blood vessels.

of suspected primary tumor of the liver should be explored, and surgical resection should be attempted in all localized liver tumors without evidence of involvement of adjacent organs or too much of the liver itself. When the left lobe is involved, the procedure of choice is lobectomy, to allow a maximal excision of tumor, permit suturing through normal tissue, take advantage of the possible physiologic line of cleavage and utilize the falciform ligament as a hemostatic covering for the raw surface of the right lobe, as brought out by Pickrell and Clay.[3]

It has been shown that the liver is a symmetrical organ with independent vascular supply to each lobe; with abundant anastomoses insuring adequate circulation if a section is cut off from its normal blood supply;[6] and with rapid regeneration after removal of its substance.[7, 8]

The control of hemorrhage has been the greatest consideration in surgical resection of liver tumors, and several methods of hemostasis have been devised. The majority of patients with hepatoma have a prior cirrhosis which aids the retention of sutures. With care, and with the use of rather thick sutures and smooth, non-cutting needles, the normal liver tissue can be successfully resected and sutured, as we have found when dealing with other tumors; for example, carcinoma of the stomach, with direct extension into a limited area of liver. The advent of new hemostatics[9, 10, 11, 12], such as fibrin foam, absorbable cellulose, synthetic adhesives[9, 10, 11,12], and new suture materials, such as flat tantalum bands, should lead to more frequent extensive operations for neoplasms of the liver.

SUMMARY

A case of primary carcinoma of the left lobe of the liver was subjected to lobectomy successfully. At autopsy, 23 months later, only intrahepatic tumors were found.

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PSEUDOEMBOLIC PHLEBITIS WITH LIGATION OF THE INFERIOR VENA CAVA

A Case Report

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The case here reported represents an uncommon type of thrombophlebitis which although well recognized and described by the French, has received little attention in the American literature. It is of interest because of the mode of onset, the complete obstruction of the inferior vena cava proximal to the point of surgical approach and the end result following inferior caval ligation.

Case Report: O.K., male, age 56, admitted to The Graduate Hospital 7/15/46, having been transferred from another hospital where he had been under treatment since 7/11/46. His chief complaint on admission was painful, swollen legs. His family history was negative. His past medical history revealed pneumonia, complicated by myocardial infarction in March, 1946, and an acute right subdeltoid bursitis in June, 1946. He had made a satisfactory recovery from both conditions.

His present illness began on July 7, 1946, when he first noticed vague aches and pains in the region of his right groin. These pains continued and became slightly more marked during the following two days. On the second day after onset (July 9) the patient was seized with excruciating pain in the right leg, and a dark congested color developed. He became so weak that he fell to the floor. At this time, according to the referrjng physician, the limb was very ecchymotic, swollen, cold and no pulsations could be felt in the femoral or dorsalis pedis arteries. His leg was very tender in the region of the ham string muscles and the muscles were spastic. The reflexes were decreased and the pain was so severe that opiates were required. At this time, his temperature was elevated to 99.4°. During the next two days, the severe pain in the right leg continued and the swelling increased very rapidly. On July 11 (the day of admission to the other hospital), the patient had a similar, but less severe attack of pain in the left groin and the left leg began to be involved in a similar process. During this time his temperature averaged about 101°.

A summary of the patient's clinical course during his stay in the other hospital revealed the following: Physical examination on July 12, was negative except for the following findings. "The abdomen is moderately distended. There is a little resistance in both lower quadrants. The entire right thigh is swollen from Poupart's ligament to the knee. There is some tenderness in the left groin, where one feels several enlarged lymph nodes. There is distinct tenderness in the right groin. The swelling described above is general and fails to localize. There is no evidence of venous engorgement and the circulation is apparently intact as the blood vessels can be satisfactorily palpated."

Laboratory findings were as follows:

7/12/46 *Urine.*—Alkaline, clear, specific gravity 1.024, albumin 3 plus, sugar negative. Microscopy reveals a moderate number of hyaline casts and an occasional coarsely granular cast, occasional leukocytes and a few squamous epithelial cells.

Blood count.—Hgb. 86%, R.B.C. 4,110,000, W.B.C. 22,500, segmented 77%, immature 6%, lymphocytes 9%, monocytes 8%.

Blood sugar.—40 mg. per 100 cc. of blood.

Prothrombin time.—Last night, July 11, 35 seconds. This A.M. 1 minute, 5 seconds.

7/13/47 *Platelet count.*—R.B.C. 4,470,000, platelets 150,000 W.B.C. and Differential: W.B.C. 23,050, segmented 81%, Prothrombin time 3 minutes.

7/12/46 *Electrocardiographic report.*—Left axial deviation. QRS2 slurred.

Conclusions.—Myocardial damage. Left hypertrophy.

Dicumarol therapy was instituted on the evening of July 11th. The following schedule of dicumarol therapy had been given before admission to the Graduate Hospital:

7/11/46	Dicumarol	200 mg.
12	"	400 "
13	"	400 "
14	"	200 "
15	"	200 "

In spite of a rapid and extreme dicumarol response, measured by a prothrombin time of one minute, five seconds on July 12th, and three minutes on July 13th, the patient's condition, as evidenced by increasing edema, rapidly deteriorated.

Physical examination after admission to the Graduate Hospital on July 15, 1946, was negative except for findings in the abdomen and lower extremities. At this time there was marked edema of both lower extremities and of the abdominal wall up to the level of the umbilicus. Acute swelling was also noted in the region of the left knee joint. The skin over this area was reddened and the local temperature increased. Marked tenderness was present throughout both lower extremities, particularly in the region of the inguinal ligaments. Severe pain was produced by the slightest attempts at passive motion of the lower extremities.

On July 16th, the following note was made by Dr. Lisker, of the department of peripheral-vascular disease. "The history suggests an occlusion of the pelvic veins, probably at the level of the common iliacs or the inferior vena cava. The occurrence of bilateral effusions in both knee joints suggests an infection as the cause of the phlebothrombosis. I recommend ligation of the inferior vena cava with aspiration of any clots found above or below this level. The prothrombin time, while delayed beyond anything I have ever seen, cannot be considered a contraindication to immediate surgical interference, since this is an emergency. The condition of the blood (prothrombin time) can be corrected with whole blood or plasma preoperatively. There is no evidence of interference with the arterial circulation."

Laboratory work at this time revealed the urine to be entirely normal. R.B.C. 3,790,000, Hgb. 63%, Leucocytes 13,000. Neutrophiles 85%, Eosinophiles 3%, Monocytes 2%, Lymphocytes 10%. Prothrombin time 9 minutes. Clotting time 5 minutes 15 seconds. Wasserman negative. B.U.N. 19 mg. Total protein 6.48. Albumin 3.98, Globulin 2.50

Roentgenogram of the chest. 7/16/46.

The examination of the chest shows the bony thorax and diaphragms to be negative. The heart shows moderate left ventricular enlargement and aneurysmal dilitation of the ascending aorta. The arch and descending aorta show only slight widening. A slight haziness is noted over the right dome of the diaphragm which might be due to either a resolving pneumonitis or a shallow respiratory phase.

Operation.—The patient was typed, cross matched, and a transfusion was started immediately. The patient was then taken to the operating room and under spinal anesthesia (procaine) a transverse incision was made 2 cm. above the right anterior superior spine of the ilium. The peritoneum was carefully displaced forward with due regard to the right ureter and spermatic vessels and the inferior vena cava was exposed. The plexus of the lumbar veins lying in the groove between the ilio-psoas muscle and the inferior vena cava was tremendously dilated. This caused considerable difficulty in exposing the vena cava and was the source of some troublesome bleeding. The inferior vena cava was carefully separated from the aorta and surrounding structures for a dis-

tance of 1½ cm. Two No. 8 silk untied ligatures were placed about the inferior vena cava about 2 cm. apart. The inferior vena cava was then opened between the two ligatures and free bleeding occurred from the distal end, but no bleeding occurred from the proximal end. The ligature distal to the opening in the inferior vena cava was then tied securely. Suction was applied within the lumen of the vena cava proximal to the point of opening and a large mass of blood clot was removed from a point at least seven or eight cm. above the opening in the inferior vena cava. The clot removed consisted of a large white organizing thrombus roughly 2 cm. in diameter, with red thrombi on its surface. The site of obstruction was very close to the point of entrance of the renal veins. Following this, free bleeding occurred from the proximal end of the vena cava and the proximal ligature was immediately tied. During this procedure the vena cava had been almost completely divided. Both ends were then secured by transfixion ligatures of No. 8 silk. The wound was closed leaving a Penrose drain in the retroperineal space. 500 cc. of blood and 900 cc. of plasma were given during the operative procedure. The patient was returned to his bed in good condition.

Postoperative course.—The patient returned from the operating room in good condition. The foot of the bed was elevated and Ace bandages were applied to both legs from toes to groins. No change in the amount of edema was noted for five days after operation.

The blood urea nitrogen which was 19 mg. on the day of operation had risen to 34 mg. on the following day, but returned to 18 mg. within two days.

The prothrombin time fell from nine minutes on the day of operation to one minute on the following day, but remained at this level, in spite of transfusion and plasma administration, until the sixth postoperative day, when it was 22 seconds. It became normal—13 seconds—on the eleventh postoperative day and the coagulation time was two minutes and fifteen seconds.

During the evening of the fifth postoperative day, there was free bleeding from the operative wound. This was controlled by packing the wound, large doses of Vitamin K intravenously and transfusions of whole blood.

Immediately after operation (2 days) paralysis of the left radial nerve was noted. This was thought to be the result of the patient's position on the operating table. This cleared during the hospital stay.

By the thirteenth postoperative day the edema of the legs had almost disappeared. The patient was allowed out of bed.

He was discharged twenty-three days after operation with supporting bandages on both legs. Only moderate ankle edema was present at this time.

COMMENT

Pseudoembolic phlebitis or the "Blue Phlebitis of Gregoire" is an uncommon type of venous occlusion characterized at the onset by a degree of reflex arterial spasm so great as to suggest embolism of a major artery. The onset is dramatically sudden with severe pain and collapse. The limb becomes cyanosed and chilled and there is absence of arterial pulsations. This is followed by the rapid onset of edema.

It is worthy of note that of the four cardinal symptoms and physical signs, namely pain, cyanosis, chilling and edema, only one, edema is of venous origin. The remaining three are due to an extreme degree of concomitant arterial spasm. The blue discoloration, previously attributed to venous obstruction is correctly described by Gregoire as being due to asphyxiation incident to an inadequate supply of arterial blood. Numerous cases have been

reported in which this arterial spasm was so severe and prolonged as to lead to gangrene of the extremity without actual occlusion of the artery.

An understanding of the mechanism involved in this type of phlebitic disease emphasizes the role of sympathetic block in its treatment. The prognosis at best is extremely grave. Early recognition with appropriate use of sympathetic block may well be the means of saving the limb or even the life of the patient. The arterial phase, as in the case here reported may be relatively short and be followed by the changes more universally recognized as due to primary disease of the venous system.

This case did not come under our observation until after the period of intense arterial spasm. It had however progressed rapidly to the point of inferior caval occlusion in spite of more than adequate anticoagulant therapy. Although no embolic phenomena had as yet occurred, it was decided after consultation with the department of peripheral vascular diseases that immediate surgery was indicated. The patient seemed to us to be in great danger of one of two fatal complications. A massive pulmonary embolus might occur at any moment, or the thrombotic process might reach and occlude both renal veins.

It is interesting to note that this patient had received adequate anticoagulant therapy in another hospital during the four days previous to his admission to the Graduate Hospital. On the morning of operation his prothrombutinton was nine minutes, and the coagulation time, five minutes and fifteen seconds. In spite of this, the thrombotic process had progressed rapidly to a critical point. Attempts to control this by blood and plasma transfusions, did not bring a satisfactory response until six days after operation. Although there was a marked prolongation of prothrombin time to nine minutes, hemorrhage was not a serious problem at operation. A moderate amount of bleeding from the wound, which occurred on the fifth postoperative day, was satisfactorily controlled by packing in the wound and transfusion.

We should also like to refer further to the technical difficulties involved in this particular case. The plexus of lumbar veins, lying between the mesial border of the iliopsoas muscle and the inferior vena cava, was tremendously dilated because the point of complete obstruction was seven or eight centimeters proximal to the area of surgical approach. Isolation of the inferior vena cava in this circumstance was a difficult and tedious dissection that required some enlargement of the original incision.

When the vena cava was opened a moderate amount of bleeding occurred from the distal end, indicating that both common iliac veins were not completely obstructed. No bleeding occurred from the vena cava proximal to the point of surgical approach. The large thrombus previously described, was removed from the inferior vena cava by suction at least seven centimeters above this point following which profuse bleeding occurred. The proximity of the process to the renal veins is at least suggested by the rise in blood urea

nitrogen to 34 mg. on the day following operation. Fortunately, this returned to 18 mg. in two days.

The clinical course following operation is also of interest. The ligation was performed on July 16, 1946, and the patient was able to leave the hospital on August 8, 1946, with a moderate amount of edema of the lower extremities. Examination in November, 1946, in the peripheral vascular department, revealed moderate edema below the knees in both legs. The patient was able to be about normally with the aid of supportive bandages to both limbs. By January, 1947, he had only slight ankle edema, little evidence of dilation of the superficial veins and was able to resume his usual occupation as a railroad engineer.

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CHOLEDOCHO-DUODENO-JEJUNAL INTUBATION FOR FEEDING FOLLOWING CHOLEDOCHOSTOMY

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VERY OFTEN FOLLOWING CHOLECYSTECTOMY and much more often following choledochostomy patients are bothered for days by vomiting. Moreover these patients are generally obese, making venoclysis difficult. The following method of feeding is presented in order to simplify the postoperative care of these patients.

A Number 6 French ureteral catheter with a fairly supple stylet in place is passed through a number of 16 French, or larger, T-tube, leaving only a centimeter of the catheter visible above the end of the long limb of the T-tube. With the common duct open, the distal end of the catheter is then threaded through the common duct, through the ampulla of Vater into the duodenum. After the direction of the catheter is down and the catheter has passed to the junction of the second and third portion of the duodenum, the stylet is withdrawn so that the bowel will not be punctured. The catheter is then passed around into the jejunum. The medial limb of the T-tube passes on into the common duct with the catheter, and if desired the end of the T-tube will easily follow the catheter through the ampulla of Vater into the duodenum. The lateral limb of the T-Tube is then put in place and the common duct sutured. The remainder of the operation is carried out as usual.

After the wound is closed and dressed, a needle hole is made about four centimeters from the end of the protruding limb of the T-tube, and, by stretching this part of the T-tube over the end of the catheter, the open end of the catheter may be brought out through this hole and the hole closed with rubber cement and a glove patch. This aids in keeping bile from draining onto the dressings. Here care must be used not to dislodge the portion of the T-tube in the common duct. A 19-gauge needle is then passed into the open end of the catheter, anchored with adhesive, and a regular clysis outfit attached to the needle. Fluids may then be given as needed, preferably continuously, by regulating the number of drops per minute so that the desired fluid will go in over a 24-hour period. Minerals, vitamins, proteins, and soluble drugs may be given through the catheter. Amigen has been used for the protein in this group of cases because it would not clog the catheter and because it was available. Giving 2,000 cc. of amigen daily over a three of four day period will sometimes cause a diarrhea which can be controlled with paregoric. After a day's rest, the amigen may be started again if needed. The bile collected by way of the tube may be strained through fine gauze, diluted with saline, and given back through the ureteral catheter.

Case 1: Mrs. M. was admitted with obstructive jaundice. The common duct was explored and a T-tube put in place. The follow up choledochogram showed a persistent filling defect in the common duct, necessitating further exploration. A ureteral catheter

was passed down the sinus tract into the common duct to facilitate identification of the common duct. The catheter passed easily through the ampulla of Vater into the duodenum and on to the jejunum as verified by roentgen-ray. With the catheter in place the common duct was easily identified and opened. As a stone could not be found, the duodenum was opened and by means of the catheter the ampulla of Vater was easily identified and incised. Upon completion of the exploration a T-tube was sutured into the common duct beside the ureteral catherter and the end of the catheter and T-tube brought out through a stab wound in the flank. Following the original operation the patient had vomited almost continuously and the fact that she had very bad veins made it difficult to feed her properly, so the catheter was left in as an aid in feeding her. She also had Wangersteen's suction in place to protect the wound in the duodenum. She was successfully fed through the catheter for 15 days following the second operation, after which time the catheter and T-tube were removed and she was able to take and retain nourishment by mouth. On the second postoperative day she developed a pneumonia which was treated successfully by giving sodium sulfadiazine through the ureteral catherter. Acidosis was combated by giving one-sixth molar Sodium R-Lactate solution through the catheter. She received 2,000 cc. amigen daily through the catheter and on the fourth postoperative day developed a diarrhea which was controlled with paregoric given through the tube. Amigen was started the following day and she was not again troubled with diarrhea.

FIG. 1.—Photograph of T-tube with ureteral catheter following removal from Case 5.

Case 2: Mrs. P. On the sixth post-partum day it became necessary to do a choledochostomy for removal of a common duct store because of progressive obstructive jaundice. Following removal of the common duct stone, a number 5 French ureteral catheter was passed through the T-tube and inserted through the common duct as previously described. Besides 10% glucose, minerals, and vitamins, she received 2,000 cc. of amigen daily through the ureteral catheter. Diarrhea developed on the third postoperative day; this was controlled with paregoric given through the catheter. Following this only enough amigen was given to keep the plasma proteins within normal limits. The patient started taking food by mouth on the fifth postoperative day and on the tenth postoperative day the T-tube and catheter were removed. On the sixteenth postoperative day she was discharged from the hospital with a completely healed sinus tract.

Case 3: Mrs. G., a 77-year-old white woman, at operation was found to have a small hobnail liver. The cirrhosis was thought to have been caused by a large nonobstructive common duct stone. After the removal of a portion of the jejunum and the completion of an aseptic end-to-end anastomosis, the stone was removed from the common duct. A T-tube with the ureteral catheter was put in place as described above and the common duct closed. On the third postoperative day she developed an oliguria with some edema of the dependent tissues. Her plasma protein was found to be 5.04 Gm. The low protein was thought to be due to faulty liver metabolism. She was given 600 cc. of blood plasma daily for four days, bringing her plasma protein up to 6.8 Gm. On

the fifth postoperative day her output of urine was normal. At the time the blood plasma was started, 10% glucose was given through the ureteral catheter, as it was thought that there would be some absorption of fluids through the jejunum proximal to the site of anastomosis. For two days the fluid aspirated through the Wangensteen suction was equal to that given through the ureteral catheter. The stoma then began

FIG. 2.—Choleodochogram of Case 2. Syringe is end of T-Tube and needle is in end of catheter.

to function and the Wangensteen suction was discontinued. On the fifth day of intravenous plasma protein she developed a rather severe anaphylactic reaction. Her plasma protein level was thereafter maintained by amigen given through the ureteral catheter, as she still had a tendency to vomit any food and most oral medication. She did, however, retain most of the choline and methionine given by mouth. No attempt was made to give this through the catheter. Her plasma protein on the fourteenth postoperative day was

6.7 and she was retaining some food given by mouth. It was interesting that when there was increased jejunal intralumenal pressure, the flow of fluid through the catheter became slower and at times stopped with escape of gas through the catheter as demonstrated by the flow of bubbles up through the infusion bottle. The T-tube and catheter were removed on the fourteenth postoperative day, and on the following day the patient got out of bed.

Case 4: Mrs. W. was admitted with progressive obstructive jaundice with a subacute cholecystitis. Following choledochostomy the T-tube with a number 6 French ureteral type of catheter was put in place. Fuids were started immediately through the catheter on the return of the patient to her bed. Because of a low blood pressure immediately following operation 1000 cc. of fluid was given intravenously, and other than this no other intravenous fluids were given postoperatively. On the third postoperative day the bile flowing through the T-tube had assumed a normal color and it was collected, strained, and given back to her through the ureteral catheter. She was gotten out of bed on the fourth postoperative day and on the fifth postoperative day was taking fluids and food by mouth. On the sixth postoperative day fluids, proteins, minerals, vitamins, and bile through the ureteral catheter were discontinued. Her convalescence was uneventful.

Case 5: Miss L. had a cholecystectomy for stones and exploration of the common duct showed it to contain much sand-like material. A ureteral type catheter was used to irrigate the larger hepatic ducts and common duct until it was thought all these particles had been removed. Following this a T-tube with a number 6 French ureteral catheter was put in place and the common duct sutured over the T-tube. Fuids, minerals, vitamins, and proteins were started through the ureteral catheter immediately on her return to bed. Intravenous fluids were not needed or used postoperatively in this case. On the second postoperative day she was taking fluids and food by mouth. On the fifth postoperative day she was taking sufficient fluids and food by mouth and fluids were no longer given through the ureteral catheter. Her convalescence was uneventful.

Case 1 has been followed for eleven months and Case 2 for five months and both are in good health with no demonstrable ill effects from the use of the catheter. The last three cases have been done in the last month and to date there are no demonstrable ill effects from the use of the catheter. In the first three cases a number of 5 French ureteral radio-opaque catheter was used; in the last two cases a number 6 French radio-opaque catheter. Radio-opaque catheters were used so that their position could be checked by roentgen-ray. In one of the cases using a number 5 French catheter (this catheter had been previously used) the flow of amigen at times was not so rapid as desired, and for that reason number 6 French catheters were used in the last two cases. Other liquid proteins can probably be administered by this method.

SUMMARY

A simplified method for adequate feeding of patients following choledochostomy by choledocho-duodeno-jejunal intubation through the use of a ureteral catheter has been presented. It has also been demonstrated that no ill effects nor delay in oral feeding is caused by this method.

CARCINOMA OF THE PREMENOPAUSAL BREAST

Endocrine Influence Suggested Clinically in 31 Cases

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FOR MANY DECADES efforts have been made to associate features of ovarian functions with adenocarcinoma of the breast. In animal experimental work many authors have shown ovarian factors to play major roles in the onset and development of breast neoplasia, but no definite correlation has ever been proven between their findings and human cases.[1, 2] The symbiotic effects of estrogenic substances on animal strain susceptibility suggests some correlation in cases such as those to be reported.

Clinically, a reverse ovarian effect has been shown by the reported palliation from oophorectomy in breast malignancy. That this effect has been greatest in premenopausal cases would be expected. Actual carcinogenic effect by administration of estrogens has been suggested only in reports of breast malignancy occurring subsequent to ovarian therapy.[3, 4, 5, 6] Such reported cases have been few in comparison to the widespread administration of these endocrines, and generally are imbued with the idea of coincidence. This is not justified if susceptibility to breast malignancy is an individual factor in each patient, as is shown to be the case with animal strains. On such a basis, the variable effect of estrogen administration would be expected. The following case studied at this hospital suggested an association between ovarian factors and adenocarcinoma of the breast:

Case 1, N.K., E.F.S.C.H. No. 3565: *History.*—This 44-year-old white woman was admitted to the hospital on December 8, 1941, stating that 6 months previously she consulted a local physician because of beginning irregularity and oligomenorrhea, with severe nervous tension. There were no signs or symptoms of pathologic alterations in the breast at that time. She was given 20,000 I.U. of theelin over a 3 weeks' period. In August, both breasts simultaneously became hard and painful and the following September she was given 75,000 more I.U. of theelin (15,000 weekly). At that time, the breasts showed diffuse tender nodularity. In November, small subcutaneous nodules appeared throughout both breasts and the patient was sent to this hospital with a diagnosis of probable cystic mastitis.

Admission Examination.—The patient was a fairly well-developed, well-nourished female. Both breasts were small, firmly nodular, with the nipples retracted and holding their position when the patient was recumbent. Numerous small rounded subcutaneous nodules were noted in the skin about the breasts (Fig. 1). The axillary nodes were bilaterally palpable and firm, but small. The liver edge extended 5 fingerbreadths below the costal margin. The pelvic examination was not remarkable. Roentgenologic studies revealed widespread osteolytic metastasis involving ribs, vertebrae, pelvis, and cranium. Biopsy of the breasts was diagnosed as carcinoma, possibly of acinar origin (Fig. 2).

Subsequent Course.—The patient was discharged from the hospital on December 12, 1941 with a hopeless prognosis. On February 13, 1942 she returned to the clinic with jaundice of four week's duration and an icteric index of 40. An attempt to perform a palliative cholecystojejunostomy failed because of metastatic spread along the biliary tree, including extensive involvement of the liver and gall bladder. Liver biopsy revealed

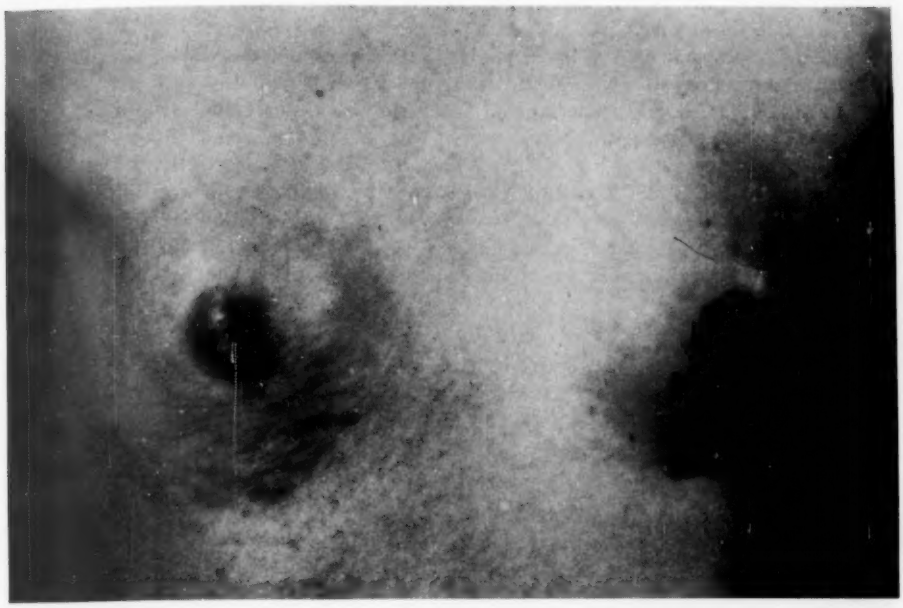

FIG. 1.—Case I. Bilateral diffuse adenocarcinoma of the premenopausal breast with generalized dissemination. (Admission photograph.)

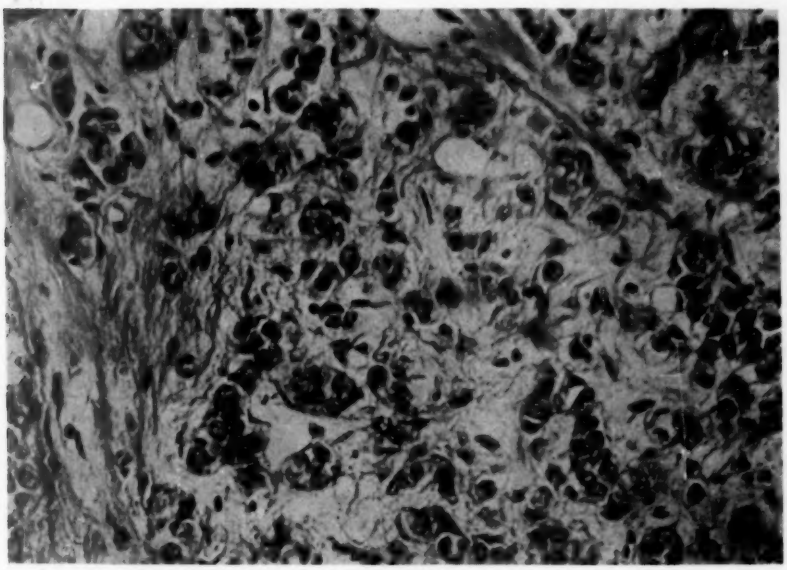

FIG. 2.—Case I. Photomicrograph (high power). Biopsy of breast parenchyma, showing adenocarcinoma of probable alveolar origin.

extensive replacement by tumor tissue. Limited exploration suggested a generalized peritoneal spread of the tumor. The patient recovered from the laparotomy and returned home as a terminal case.

To the amazement of the Staff, she returned for a clinical checkup on August 14, 1942, exhibiting general clinical improvement with weight gain and regression in breast size (Fig. 3). The icteric index was 7. This improved state continued until January 1, 1943 when she returned with ascites, weight loss, paraplegia, and roentgen evidence of pulmonary metastasis. In July 1943 these symptoms had all progressed, and the patient expired on September 8, 19 months after having been clinically in a terminal state of her malignancy.

AUTOPSY EXAMINATION: *Gross Findings.*—The breasts appeared bilaterally atrophic, nodular, and fibrotic. Examination of the thoracic contents failed to reveal any evidence

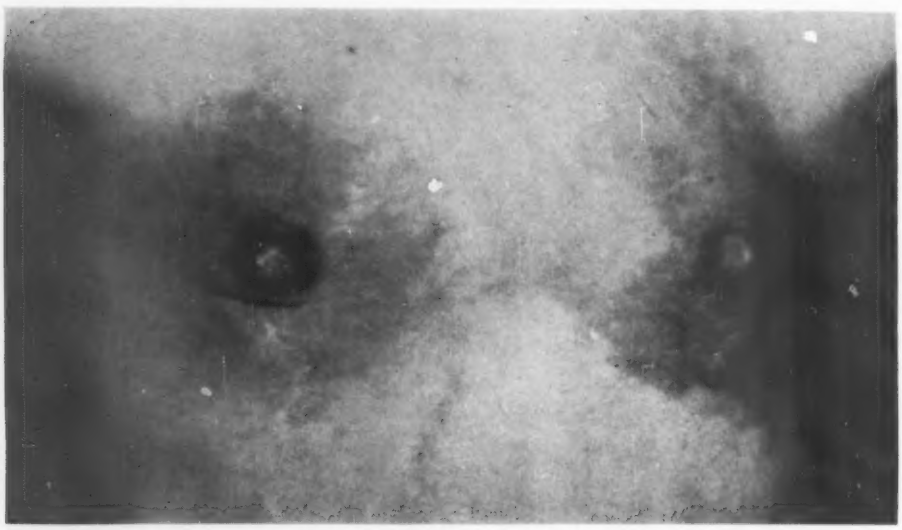

FIG. 3.—Case I. Note spontaneous regression in size of both breasts. (8-months follow-up.)

of tumor metastasis. Each pleural cavity contained approximately 300 cc. of clear straw-colored fluid. The peritoneal cavity contained 1000 cc. of bloody fluid and revealed innumerable small tumor implants. The liver weighed 1,120 Gm. and was almost completely replaced by tumor metastases. Several lumbar vertebrae were replaced by grayish-white tumor tissue. The ovaries together weighed 30 Gm. and were diffusely involved. Metastatic adenopathy was not present in either the axillary or supraclavicular areas.

Microscopic Study.—The tumor from the breast was composed of masses of tumor cells with some attempt at adenoid arrangement. Individual cells varied considerably in size and shape. They were uniformly quite irregular, with prominent nucleoli and pale pink cytoplasm. Infiltration was present in the surrounding breast and fat, and in areas of tumor growth the normal breast parenchyma was obliterated. Variable amounts of connective tissue stroma were present around the tumor and many small nests of tumor cells were present in lymphatics. It suggested acinar epithelial origin. The liver substance was diffusely replaced by tumor tissue which was also present in the wall of the gallbladder and in lymph nodes around the porta hepatis. The spleen and both lungs showed metastatic foci. Bone marrow of the ribs and vertebrae was extensively implicated by tumor. Both ovaries showed complete loss of ovarian substance by replacement with tumor tissue.

COMMENT

It was felt that this case presented two phases of possible ovarian influence on the breast malignancy: first, the sequence of the original bilateral painful swelling of the breasts for four to five weeks, following the administration of estrogen substance. The second course of therapy was followed by an atypical bilateral diffuse malignancy originating from acinar epithelium of the breasts and associated with a generalized metastasis. These changes all occurred within the six-months period of theelin therapy which had started with clinically negative breasts. Secondly, the regression of the hopeless picture of generalized metastases, biliary obstruction, and hepatic damage observed in February 1942, followed by progressive improvement for 10 months, was thought to be explained by the loss of ovarian substance which occurred with the peritoneal spread.

The theory of an endocrine factor in premenopausal breast malignancy has its maximal support in the cases associated with the administration of hormonal therapy. However, the occurrence of such a combination is too infrequent to offer significance except perhaps as it applies to the individual case. Any hormonal influence which would be present in the majority of such cases would necessarily be as an endogenous factor.

On this basis, a study was made of all breast malignancies in patients under 50 years of age who were admitted to The Ellis Fischel State Cancer Hospital prior to 1946. Since this represented only a clinical study, specific endocrine factors could not be evaluated accurately; the evaluation was made on the endocrine balance as a whole picture. This series includes 39 cases; 30 of these presented fairly definite clinical evidence of deviation from a normal hormonal balance.

TABLE I

39 Cases were studied:

GROUP A.—25 were still in their normal menstrual life at the time of diagnosis of their tumor. Of these:

1. 16 (average age 46) gave menstrual histories of marked irregularity; including menorrhagia, oligomennorrhea, etc., dating from 5 to 28 years.
2. 9 Gave normal menstrual histories without difficulties. However, the age of this group still in active menstrual life averaged 49.8 years.[7]

GROUP B.—5 associated their growth's appearance with the onset of menstrual abnormalities, menorrhagia, and/or metrorrhagia of a duration of 2 to 16 months.

GROUP C.—9 had undergone surgical termination of menses prior to the onset of their tumor.

While a fairly definite abnormal endocrine pattern was suggested in groups A-1 and B, Group C, forming 24 per cent of the total premenopausal cases, was the most suggestive of such an influence.

TABLE II.

Patient	Operative Age	Operative Procedure	Age of Appearance of Breast Carcinoma	Follow-up
1	47	Complete hysterectomy +(?) for dysmenorrhea; menometrorrhagia	51	Inoperable
2	39	Complete hysterectomy and oophorectomy for cervical carcinoma	48	Recurrence and death.
3	26 40	Left ovary removed for cyst. Right ovary removed for menorrhagia	46	Inoperable
4	35	Operated for fibroids (?). Menopausal symptoma followed	50 (left breast) 51 (right breast)	1 yr. post operative without recurrence
5	24	Operation (?). Menorrhagia. Cessation of menstruation.	39	Recurrence and death
6	31	Left ovary and uterus—cause ?	51	Inoperable
7	42	Menometrorrhagia. Operation done (?)	51	2 yrs. post operative with recurrence.
8	31	Pelvic operation. Cause (?). Operation (?). Cessation of menstruation.	51	Inoperable
9	36	Dysmenorrhea and irregularities	38	1 yr. post operative without recurrence. Opposite breast presenting marked nodularity.

The variety of operative procedures which these patients received would preclude any correlation of a resulting effect. The presenting dysfunctions listed as necessitating surgical intervention all parallel the idea of a pre-existing severe endocrine imbalance. It would not be expected that such a hormonal pattern would be corrected by a surgical menopause.

CONCLUSION

The specific factors in the pattern of a malignant process remain unknown. It has been suggested by the cases presented that breast susceptibility to such a cellular change may be a variable, modified by the endocrine pattern. Clinically and pathologically our premonopausal group exhibited a virulent neoplasia, frequently including acinar epithelial elements, and associated with an endocrine pattern varying from physiologic normalcy. A promient group of our cases presented a history of endogenous endocrine dysfunction, requiring previous surgical menopause. While the effect of estrogen administration cannot be evaluated accurately in its relation to premenopausal breast malignancy, it appears significant in the case presented.

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BOOK REVIEW

"The Aseptic Treatment of Wounds"

By CARL W. WALTER, M.D., THE MACMILLAN COMPANY, NEW YORK.

The publication of this important work marks an epoch in the history of surgery which competes in importance with many of the events in the evolution of asepsis outlined by the author in his opening chapters. Bringing to his subject the combined knowledge of the surgeon and the engineer, Dr. Walter has assembled in this volume the results of a decade of research and systematic compilation of data on the technology of asepsis. The title was selected for historical reasons as a tribute to Curt Schimmelbusch, who published in 1893 the first monograph on aseptic technic entitled "The Aseptic Treatment of Wounds," from which the first chapter of the new book is a verbatim quotation. However, in choosing this title the author has failed to convey a true indication of the breadth and encyclopedic detail of its content.

Starting with a comprehensive historical review of antiseptic and aseptic surgery, the author then discusses from scientific, technologic, and practical viewpoints the destruction of bacteria by chemical and physical agents. The thermal and bacteriologic characteristics of heat sterilization are presented in great detail, much of the data being derived from the author's own authoritative research in this field, and specific technics are described for sterilization of each item of equipment employed in the operating theater. The usefulness and limitations of chemical disinfectants in sterilization of instruments and skin are thoroughly considered. Full bibliographic references are supplied for each topic and constitute one of the most valuable features of the book. All of the procedures connected with provision of a sterile operative field, including the design and packaging of kits, the treatment of skin of patients and personnel, the control of air borne infection, the draping of the patient, and the wearing apparel of the surgical team, are taken up in clear and orderly fashion and illustrated by a profusion of excellent line drawings.

The concern which the author displays for preservation of the life of materials and instruments will be welcomed by the hospital administrator. The surgical chief and the operating room supervisor will find this book a standard reference by which to judge, in their own hospitals, the adequacy and efficiency of technics which may be rooted in fad and fancy rather than in the solid scientific data which support Dr. Walter's recommendations. He again goes beyond the limits of his title in his chapters on "Preparation of Parenteral Fluids" and "Blood and Plasma Facilities," but the hospital staff committee harrassed by an outbreak of infusion and transfusion reaction will be grateful to find the probable answer to their problem in this section. The hospital plumber or sanitation engineer will also have occasion to refer to this volume in connection with the maintenance and operation of sterilizing facilities and plumbing equipment. It may be hoped that the publication of this book will prompt the personnel of each and every hospital to re-examine its equipment

and its manual of procedures, and *its practical use thereof*. Careful observance by the hospital staff of the principles and practices outlined in this monograph will leave to the individual surgeon the inescapable and undivided responsibility for the quality of healing of his clean oerative wounds.

However efficient the modern complex hospital organization may be, it does not possess the "aseptic conscience"; that is a personal quality of the individual surgeon and nurse and must be inculcated into every potential member of an operating team through intelligent teaching and precept. Here is a superb text for this purpose.

JOHN S. LOCKWOOD, M.D.

LETTERS TO THE EDITOR

DEAR SIR:

The article entitled "Patho-physiology of the Cause of Death from Coronary Thrombosis," by Gordon Murray, which appeared in the October, 1947, issue of the ANNALS OF SURGERY, requires comment, especially in view of the broad clinical implications drawn by the author.

1. It should be noted that a description of the mechanical changes occurring in the zone of experimentally produced myocardial infarction was published by Tenant and Wiggers in 1935 ("The Effect of Coronry Occlusion on Myocardial Contraction"—Am. J. Physiol., 112: 351, 1935). The "Paradoxical Systole" observed by Murray was recorded and analyzed in great detail by Tennant and Wiggers with the aid of an optical recording Myograph. Simultaneous pressure pulses from the aorta or left ventricle were also recorded optically. The observations made by Murray confirm, but do not extend those previously made by Tennant and Wiggers. No acknowledgment of this prior work is made by Murray.

2. Although it is undoubtedly true that cardiac output will diminish in these experiments as a result of a fall in blood pressure (assuming a constant peripheral resistance), the method used by Murray for measuring left ventricular output is crude and hardly reliable.

3. It is incorrect to assume that the loss of contractility in the zone of myocardial infarction results in a state in any way similar to that which occurs following the development of a peripheral arteriovenous aneurysm. The primary hemodynamic alterations in A-V aneurysms are the result of the A-V shunt. This does not exist in myocardial infarction. It has been demonstrated that A-V aneurysms produce increased cardiac output, elevation of systolic and depression of diastolic pressure, and increased blood volume. Acute myocardial infarction results in very different, almost opposite changes.

4. The implication that practically all animals who are subjected to experimental coronary ligation die is not in accord with the fact, since it is well known that the survival rate of such preparations is about 50-75%. Control experiments are not described and referred to only obliquely.

5. The implication that infarction of the interventricular septum has a better prognosis than infarction elsewhere in the myocardium is not in accord with facts.

6. The mortality from acute myocardial infarction in human beings is 20-25% in the first 6 weeks following the clinical episode. The use of anti-

coagulant drugs may reduce this to 15-20%. Hence, the prognosis following myocardial infarction is not as poor as implied by the statement ". . . Medical treatment is so ineffective and is entirely helpless . . ." The surgical risk involved in excising a segment of myocardium from a patient with a recent myocardial infarction cannot be dismissed as glibly as does Murray and would probably far exceed the 15-20% mentioned above. Furthermore, it will be rather difficult for cardiologists to accept the undocumented statement, "The question of the anesthetic is not a serious one, because there is some evidence to suggest that a patient under ether anesthesia is in less danger with a coronary occlusion, than he is without the anesthetic."

7. Although Murray obtained an 80% survival rate following excision of the infarcted myocardium, similar experiments done by Drs. E. Sinaiko, B. Kondo and myself on a small series of dogs in the Cardiovascular Department of Michael Reese Hospital (unpublished), resulted in a mortality rate of 100%.

I believe that one should approach the clinical application of excision of an area of myocardial infarction with considerably more reserve than exercised by Murray.

Sincerely, (signed) M. R. MALINOW, M.D.
Chief of Clinical Investigations
"Pabellon Inchauspe de Cardiologia"
Hospital Ramos Mejia
Buenos Aires, Argentina

DEAR SIR:

Thank you for your letter regarding a communication from Dr. Malinow of Buenos Aires. I was glad to receive the reference in the American Journal of Physiology. I have looked this up and have noted:—That Tennant and Wiggers in their article described a very nice instrument which has been placed on the area of infarction and which demonstrated first of all the contraction and subsequently the expansion of the infarcted area during systole. They made no observations regarding the relationship of the area involved to the actively contracting muscle of the ventricle elsewhere. They made no observations on the blood pressures or on the cardiac output before and after the occurrence of infarction of a portion of heart muscle. They did not prove, as we have done, by excision of the infarcted area, that the effect produced in the general circulation of the animal and as well the cause of death, are the result of this expansion chamber, or as labelled "paradoxical systole" in the ventricle.

In my article the premises for the investigation was, as stated, 1.) To explain why patients run a low blood pressure following infarction of the heart and, 2.) Why the patients die. I think careful perusal of the article will show that the cardiac output is cut down to such an extent and the blood pressure falls to such an extent on this account that the animals are unable to survive, and the proof of this is that when the infarcted area is excised and the experiments are satisfactorily completed, the reverse is true.

Sincerely yours, GORDON MURRAY.

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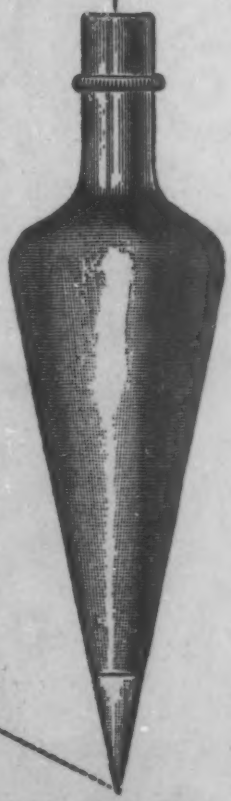
ADMINISTRATION: Employ 1 mg. of NEOcaine per pound of body weight, up to 150 mg. Dissolve crystals with spinal fluid led into the ampoule. Inject slowly with optional barbotage, using a 22 gauge needle. Contraindicated in gastrointestinal perforation, obstruction, peritonitis, severe hypotension, cerebrospinal or dorsal skin disease. Drug idiosyncrasy is rare.

SUPPLIED: Ampoules of 50, 80, 100, 120, 150, 200, 300 mg. of pure procaine hydrochloride. Boxes of 10. For continuous spinal anesthesia, ampoules of 500 mg., individually boxed.



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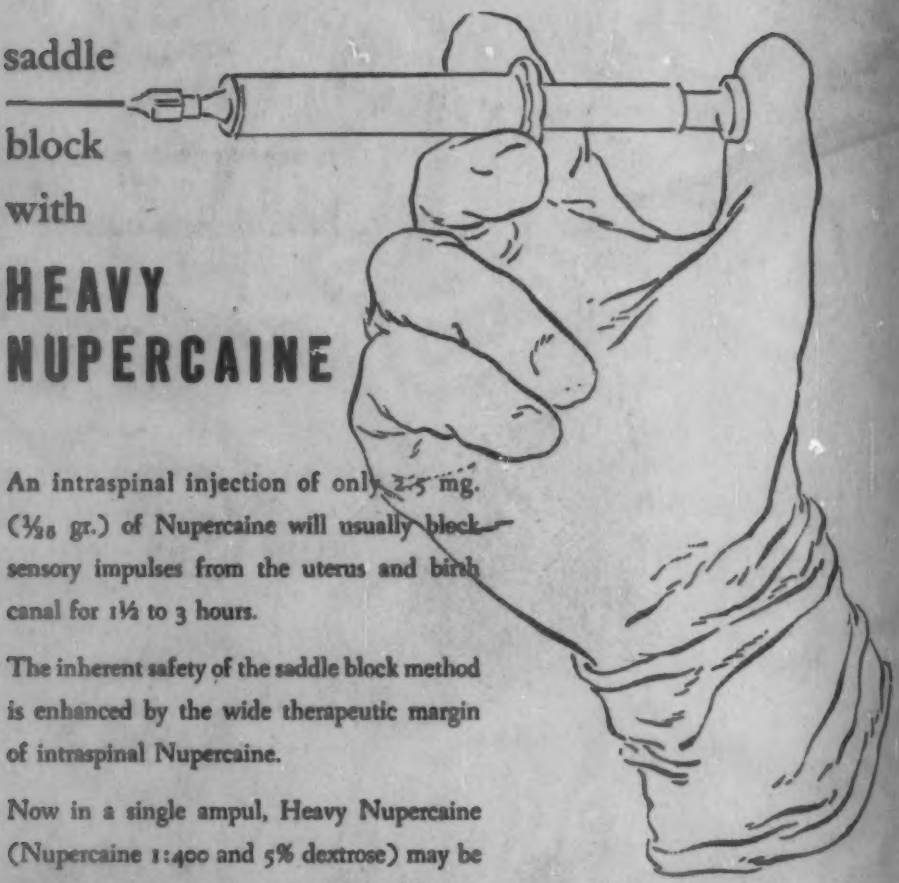

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